SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 85 DECEMBER, 1947 NUMBER 6

THE RÔLE OF VASCULAR SPASM IN RECOVERY OF STRANGULATED INTESTINE

Experimental Study

HAROLD LAUFMAN, M.D., F.A.C.S., and HAROLD METHOD, M.D., Chicago, Illinois

MANY factors are involved in the recovery of intestine of questionable viability once it has been released from strangulation. Some of these factors have been extensively investigated and will be reviewed in this report. One factor, however, which has received very little attention, but which apparently is of significance in the recognition of viability and in the recoverability of strangulated intestine, is the degree of residual spasm in the involved vascular bed. It is therefore of rather fundamental importance to investigate the train of events in the intestinal vasculature following strangulation.

The present study is mainly concerned with two aspects of the problem. The first is the development of a method of recognizing grossly the degree of vasospasm which might serve as an index to the recoverability of strangulated intestine. The second is an evaluation of present methods of resuscitation and an investigation into additional measures which could be of practical value. The importance of recognizing viable bowel and of resuscitating a borderline case to a state of viability are too well known to require emphasis at this time.

Prize Essay for 1947, Chicago Surgical Society. Read before the Chicago Surgical Society May 2, 1947.

From the Department of Surgery, Northwestern University Medical School.

PATHOLOGICAL PHYSIOLOGY OF INTESTINAL STRANGULATION FROM THE STANDPOINT OF THE INVOLVED VASCULATURE

Strangulation of the intestine occurs when the blood supply of a closed loop obstruction has been compromised. Hence, we are dealing with the combined effects of three pathological entities: closed loop intestinal obstruction, mesenteric vascular occlusion, and simple in-

Fig. 2. Appearance after release of 2½ hour arterial type strangulation, showing visible reactive hyperemia and definite evidence of viability.

Fig. 3. Appearance after release of 2½ hour venous type strangulation showing irreversible hemorrhagic infarction of loop.

Fig. 5. a, Appearance of loop in a control dog 6 minutes after release of a half-hour venous type strangulation. b, Appearance of loop 6 minutes after release of a half-hour venous type strangulation in dog treated with papaverine 3 minutes before picture was taken.

Fig. 6. a, Appearance of loop in a control dog 6 minutes after release of 1 hour venous type strangulation. b, Appearance of loop 6 minutes after release of 1 hour venous type strangulation in dog treated with papaverine 3 minutes before picture was taken.

Fig. 7. a, Appearance of loop in a control dog 6 minutes after release of 1 hour venous type strangulation. Compare with Figure 6a and note how presence of luminal contents influence viability. b, Appearance of loop 6 minutes after release of 1 hour venous type strangulation in dog treated with papaverine 3 minutes before picture was taken. Compare with Figure 6b and note more questionable appearance of bowel despite treatment when lumen contains digested food.

Fig. 8. a, Appearance of loop in a control dog 6 minutes after release of a 3 hour venous type strangulation. This loop is nonviable. b, Appearance of loop 6 minutes after release of a 3 hour venous type strangulation in dog which was treated with papaverine 3 minutes before picture was taken. No change in appearance was produced. The loop is nonviable.

testinal obstruction proximal to the strangulation. Although our main concern at this time is with the vascular element and its effect on the strangulated loop, we consider all the factors listed below as important in the delicate balance between recovery and death of involved intestine.

FACTORS CONCERNED WITH RECOVERY OF VIABILITY

1. Duration of strangulation
2. Extravasation of blood into tissues
3. Autolysis and bacterial invasion of intestinal tissue
4. Metabolic activity of tissue at time of strangulation
5. Presence of closed loop obstruction
6. Length of involved segment
7. Caliber of vessels occluded
8. Suddenness of occlusion
9. Presence of intravascular obstruction (embolism or thrombosis)
10. Degree of residual vasospasm

There are two distinct types of strangulation obstruction—the arterial type and the venous type. Various degrees of combined arterial and venous type strangulation also occur.

Arterial obstructions in their pure form probably occur clinically only in mesenteric arterial embolism or thrombosis. In what we have designated as an arterial type strangulation, the veins as well as the arteries are occluded, but the effects of the arterial occlusion are predominant. This predominance can occur only if the artery becomes occluded almost simultaneously with the vein.

The venous system is primarily occluded in most clinical forms of strangulation, such as encirclement by the mouth of a hernial sac or by adhesions, intussusception, and various types of torsion. Examples of pure venous occlusions without closed loop obstruction are thrombosis of the mesenteric veins and intestinal obstructions in which the intraluminal pressure occludes the intramural veins.

A. Arterial occlusion. Spasm of the arteries and arterioles distal to an acute arterial occlusion is a well established fact. This phenomenon has been studied extensively in sudden occlusions of the peripheral (2, 7, 14, 28, 30, 37), coronary (23, 27), and pulmonary arteries (5, 9, 10). Certain equivocal clinical observations have indicated that the same sequence follows occlusion of the mesenteric arteries (26). However, although the mesenteric and intestinal vasculature has been under investigation since the days of Virchow and Cohnheim and later, notably Mall, many aspects of its behavior under pathological conditions have remained in the realm of surmise. It remains to be demonstrated to what extent our present-day knowledge of peripheral vascular occlusions applies to occlusions of the mesenteric vessels.

In 1931, Mulvihill and Harvey showed, by means of temperature responses, that spasm is an important sequel to arterial occlusion in the leg of a dog. This spasm could be relieved by ganglionectomy. In 1932, Gosset and his associates observed that an embolus was fixed at its point of lodgment by arterial spasm. Allen and MacLean in 1935 also pointed out that the profound ischemia which results from sudden arterial occlusion is far too marked to be explained on the basis of obstruction of the lumen by the embolus alone.

Since, in an arterial type intestinal strangulation, it is possible to relieve the arterial occlusion by releasing the strangulation at laparotomy, the demonstration of spasm and its consequences is of some importance in the question of survival of the intestinal segment.

When a strip of binding tape strangulates a segment of an animal's intestine tightly enough to occlude the artery, the vein is also occluded. Under such circumstances the smooth muscle of the intestine becomes spastic due to the sudden cessation of the supply of blood and acquires a rippled appearance (Fig. 1). Microscopically,[1] we have observed that the flow of blood in the capillaries does not cease the moment the constriction is applied. But because the arteriolar pulse continues, blood continues to be propelled from the arterioles into the venules in gradually diminishing proportion until the arterial tree is practically empty and collapsed. Grossly, the pooling of the blood in the venous system is seen in the cyanotic areas between the pale, spastic areas in the intestine, the latter portions being practically devoid of blood. Thus, at this stage, the venules are relatively engorged while the ar-

[1]A detailed account of our studies in capillary microscopy comprises another report.

terioles are almost empty and in severe spasm. The metarterioles and capillaries are in varying degrees of spasm and relaxation, and the blood cells rock to and fro in some of them.

If the arterial occlusion continues, there is a gradual relaxation of the arteriolar side of the vascular bed under the influence of the local anoxia, and some of the blood will settle back into the arteriolar vessels. Lewis observed this phenomenon in the upper extremity of man. If the occlusion continues long enough, an equalization will finally occur in the distribution of the blood between the venous and arterial side. Grossly, this is observed in the intestine under arterial strangulation by a gradual relaxation following the initial spasm pursuant to occlusion and a very slow but definite turn from a blanched, pale, rippled appearance to a more homogenous cyanotic appearance. We have observed that if the occlusion remains long enough to allow this secondary relaxation to become evident grossly, the chances for recovery diminish proportionately.

If an arterial type strangulation is released while some spasm remains in the intestinal musculature, the blanched, spastic bowel becomes bright red, and the small, tight contractures give way to larger, more organized peristaltic movements, but hyperactivity of the segment persists for some time (Fig. 2, frontispiece). In general, the more prolonged the arterial occlusion, the less pronounced will be this red response. Lewis noted this train of events in the human arm, and termed the phenomenon "reactive hyperemia." This has been defined as the period in which the local circulation to an organ is increased above the control resting level following the re-entry of blood into the ischemic tissue. During the period of occlusion, the tissues have incurred a blood flow "debt" which is repaid as soon as possible after circulation is restored.

After the phase of reactive hyperemia in the intestine, there follows a secondary spasm of a mild nature which is apparently compensatory, but which may be of importance in delaying eventual recovery of the bowel. If the strangulation remains until some secondary relaxation occurs, the reactive hyperemia in the intestine is not so pronounced, or it may be absent. In such cases the color is violaceous, due to the stagnation of blood in relaxed vessels.

Fig. 1. Arterial type strangulation, left, compared with venous type strangulation after 1 hour. There has been a slight relaxation in the blanched, rippled appearance of the arterial type by now but its mesentery is still free from petechiae and the bowel is pale, whereas the venous type strangulation is distended, weeping, and blood soaked.

The mechanism responsible for the spasm and vasorelaxation of blood vessels is as yet controversial. The spasm has been ascribed to stimulation of sympathetic fibers by the occlusive irritant, while the relaxation is not dependent on the integrity of the sympathetic nerves, but is apparently related to the accumulation of chemical products of tissue anoxia (17).

B. Venous occlusion. In a venous type strangulation we are dealing with a loop which quickly becomes engorged, edematous, and blood soaked (Fig. 1). Since most strangulations encountered at surgery are of the venous type, and since it is a commonly acknowledged clinical fact that vasodilating measures such as warm packs do improve their appearance, it it would seem rather necessary that observations be made to clarify this point.

It has been shown that in the lower extremity, when acute venous occlusion by a thrombus results in a damming up of blood and an increase in local venous and capillary pressure, the magnitude of this alteration will be inversely proportional to the degree of available collateral circulation (31). It has been suggested (1) that the resistance (tone, spasm?) in the walls of the minute vessels both on the arterial and venous sides tends to cause further decreased venous circulation. All the tissues, including the capillary endothelium, suffer from

anoxia, resulting in increased capillary permeability. Coincident with changes in arterial and venous portions of the system, there is a diminution in the flow of lymph (31, 32).

Regarding the status of arterial blood flow in venous occlusion, Abramson has summarized our present-day knowledge as follows: "Some workers have found an elevated cutaneous temperature and increased oscillometric readings, while others have noted that the extremity is colder than normal. It may be that the same phase of the condition was not studied by the different authors or that the type of peripheral vascular response depends upon the magnitude and location of the site of occlusion." Other authors, notably Ochsner, are convinced that there is an unmistakable phase of arteriolar spasm following acute venous occlusions.

When binding tape is placed about a loop of intestine and its mesentery just snug enough to occlude the veins, the segment gradually becomes engorged and assumes a deep purple color. This is undoubtedly the result of damming up of blood in the veins and venules. Meanwhile, local arterial pulsations carry on in their usual manner, and for a while are actually increased in intensity. This observation is in keeping with that of Lewis, who described an exaggerated pulse volume following venous congestion in the hand. Now if we allow the strangulation to continue, we find that the arterial pulsations within the strangulated portion of mesentery become more feeble and as the tissue becomes more blood soaked, arterial pulsations can no longer be palpated. Release of the strangulation at this point (about ½ hour in short segments in the dog) will usually result in a resumption of the pulsations, a rapid disappearance of the deep cyanosis, and a bright red flush indicative of recovery of the bowel. Just before release, capillary microscopy reveals engorged venules and quite narrowed arterioles. The capillary bed is very full, but not uniformly so. Extravasations of blood cells into the tissues are seen in every field. Variations of this condition can be seen up to about an hour of venous strangulation.

After approximately one hour of venous strangulation, capillary microscopy reveals not only the venules, but most of the capillary bed to be engorged, and vessel walls are very difficult to distinguish because of the sanguineous extravasation into the tissue. The rate of blood flow through the arterioles has become markedly diminished, and the blood cells travel in clumps. Minute thrombi form easily. Although the arterioles, for the most part, are narrower than the engorged venules, there has been some relaxation by this time. As the blood is dammed up in the venous system, the arterial stream becomes slowed. This process is by no means simultaneous or uniform in all areas. This secondary relaxation of the spastic arterioles in venous occlusion occurs sooner than in arterial occlusion. Nonetheless, it seems to bear the same relationship to recoverability as in arterial occlusion. Thus, the more pronounced the secondary arteriolar relaxation due to anoxia, the poorer are the chances for recovery of circulation. Figure, 3 frontispiece, illustrates a venous type strangulation after 2½ hours. It is of very questionable viability.

In most instances a blood stained, plasma-like transudate accumulates in the peritoneal cavity, the result of increased capillary permeability.

Arteriolar spasm in some venous strangulations may conceivably result from a tightening of the constriction due to tissue edema, finally to occlude the incarcerated arteries. In such a case we have a venous occlusion with superimposed arterial occlusion. However, arteriolar spasm has been seen in pure venous occlusion without strangulation in which the main artery was free throughout the experiment.

If vasospasm occurs in the early stages of venous strangulation, increasing the arterial inflow by vasodilator therapy even in the presence of already overdistended veins should be of value provided the therapy is instituted while a sufficient degree of tone remains.

In general, whether the strangulation be arterial or venous, the prognosis for recovery is apparently inversely proportional to the degree of secondary relaxation. In venous occlusion, there is undoubtedly a changing balance between the residual tone in the smaller vessels on the one hand, and the relaxation caused by anoxia or distention resulting from engorgement, on the other.

Fig. 4. a, left, Method of taking surface temperature of intestinal loop during strangulation. b, Same procedure after release of strangulation. These readings are valid only when compared with similarly exposed normal bowel.

EXPERIMENTAL METHODS

Experimental inquiry into the clinical application of the status of the minute vessels in strangulation requires an appropriate gross measuring device. We therefore borrowed a test which has long been used in peripheral vascular disease—that of recording skin temperatures—and applied it to the serosal surface of the bowel.

Ordinary mongrel dogs were starved for 24 hours and anesthetized with intravenous nembutal. All strangulations were produced by placing binding tape about a loop of ileum. The strangulated segment was always about 8 centimeters (roughly 3 inches) long. The venous type strangulations were made by tying the tape just tightly enough to occlude the veins to the segment, but allowing arterial pulsations to come through. The bowel immediately turned purple-blue, then gradually distended. In the arterial type strangulations the tape was tightened until no pulsations could be felt in the vasa recta. We could determine the completeness of an arterial type strangulation by the blanched, rippled spastic appearance of the gut musculature. In preliminary experiments we found that a segment about 3 inches long was convenient in that it showed questionable viability after approximately 1 hour for the venous type and after 2½ hours for the arterial type. After strangulation, the loops were returned to the abdomen until time for recording surface temperatures.

Surface temperatures were taken with an ordinary skin thermometer[1] by placing the thermometer on the lateral serosal surface of the bowel and keeping it in place until the mercury came to a standstill (Fig. 4). This usually occurred after ½ to 1½ minutes. Preliminary work indicated that variations up to 0.6 degree C. may fall within experimental error, but after repeated performances this error could be reduced almost to zero. Since the intestinal surface temperature is influenced by the temperature and humidity of the air, a control reading of neighboring normal bowel, similarly exposed, was always made just before that of the involved segment. Ideally, surface temperatures should be taken on dry surfaces. When two points are being compared, however, it is more important that both should be exposed to the same conditions. To equalize the variables associated with loss of heat by evaporation, readings were always taken when the bowel was moist. In this way the difference in the degree of evaporation heat loss between the control and the involved loops was brought within satisfactory limits for our purposes. The bowel was always held in the same manner to equalize errors induced by conduction. Thus, by subjecting the normal control bowel and the involved loop to the same errors of heat loss through vaporization, radiation, convection, and conduction, our readings

[1]Both the Becton-Dickinson and Rascher-Betzold skin thermometers were used.

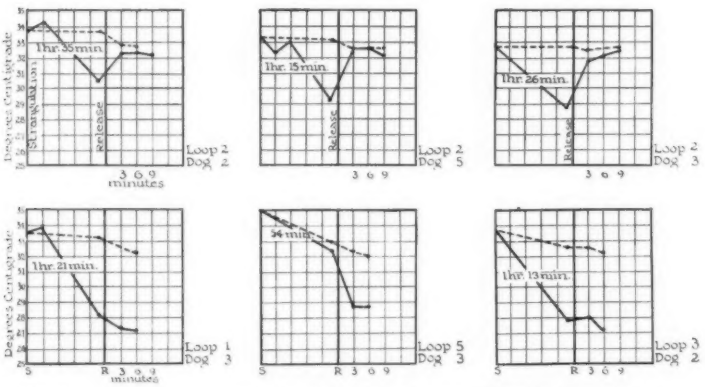


Chart 1. Temperature curves in viable venous type strangulations, above, compared with those in nonviable strangulations of the same type, below. Temperature of strangulated loop shown by solid line; control by interrupted line. *S*, Strangulation; *R*, release. Note that the duration of strangulation varies with each segment and although important within limits, does not alone determine the type of temperature response, because of the many other factors involved. These graphs indicate that if the temperature response following the release of strangulation is poor or negative, the viability of the loop is very doubtful.

could be interpreted as being accurate on a comparative basis between the two points. It was not necessary to obtain absolute readings by calculation or to use an electrical thermocouple.

INTESTINAL SURFACE TEMPERATURE IN VENOUS TYPE STRANGULATIONS

Temperature readings were made before and after release in 28 venous type strangulations. Typical curves of the surface temperature are portrayed in Chart 1. Shortly after strangulation the temperature of the loop rose slightly above that of the neighboring normal bowel in some instances. This undoubtedly was the result of initial engorgement. After 45 to 90 minutes of strangulation the temperature of the loop dropped from 1 to 5 degrees centigrade. Upon release of the strangulation, we were interested in determining whether the behavior of the surface temperature was an indication as to whether or not the segment would survive. Three minutes were allowed to elapse between the time of release and the next reading, and an equal time interval between subsequent readings. We found that in the viable segments, there was a slow rise in temperature, sometimes finally reaching that of the neighboring normal bowel, other times not quite equalling the control reading. In nonviable segments the temperature either remained at its strangulation temperature or actually declined. No resuscitative therapy was used in these animals. Our predictions were checked by postmortem examinations when necessary.

INTESTINAL SURFACE TEMPERATURE IN ARTERIAL TYPE STRANGULATIONS

Temperature readings in 20 arterial type strangulations showed a rather different response than did the venous types. The temperature began to drop almost immediately, first slowly, then more rapidly. As shown in Chart 2, temperatures dropped as much as 6 degrees after arterial occlusion. However, if the strangulation was released before the phase of secondary relaxation, that is, up to about 2½ hours for the length segment we were using, the temperature bounced up to *above* that of the neighboring normal bowel. This rebound, or reactive, hyperemia was never observed in venous type occlusions.

If the strangulation was allowed to remain until after secondary relaxation of the intestinal musculature, reactive hyperemia did not occur, and the temperature stayed at its strangulation level. Such segments were always nonviable.

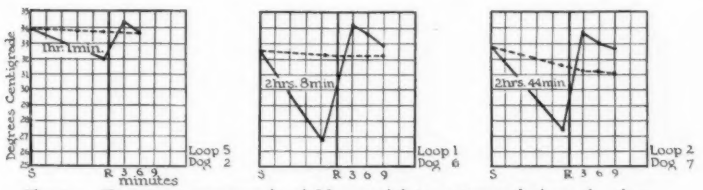


Chart 2. Temperature curves in viable arterial type strangulations showing the phenomenon of reactive hyperemia as it reflects in the temperature response following release. If an arterial type strangulation is nonviable, its temperature curve is no different from that of a nonviable venous type as shown in Chart 1.

METHODS OF RECOGNITION AND REVIVAL OF BORDERLINE CASES OF INTESTINAL VIABILITY

Oftentimes recognition of viability may prove fallacious even by surgeons of the widest experience. The tests for viability in use today include: (1) the return of pulsations to the segment; (2) the return of the pink color of viability; (3) the return of peristaltic movement; (4) the fluorescein test. Although all these tests are of value, they have certain limitations.

The return of pulsations may not always be an indication of viability. Pulsations may not be palpable, yet the segment may live. Pulsations are known to be transmitted through thrombotic vessels. Furthermore, in venous occlusions with irreversible changes in the bowel, the return of pulsations may be misleading.

The return of color resembling that of viability is not always useful as a test, since many segments with an ominous deep purple hue are known to survive. However, when the blush of viability does return, it is a fairly reliable criterion.

The return of peristalsis is a poor prognostic criterion of viability, since we know that anoxic intestine may be very active for a while. This anoxic spasm may be erroneously interpreted as active peristalsis.

The fluorescein test, first employed by Lange and Boyd in 1942, is probably the best test of viability we have to date. It is unquestionably accurate (15), but has its drawbacks. We think it a fair assumption that most surgeons would rather go ahead and resect a questionable segment of bowel than darken the operating room, use a special ultraviolet lamp with a Wood filter, and inject a solution of fluorescein and sodium bicarbonate intravenously into the patient.

Recent developments in isotopic tracer substances fire the imagination with possibilities of using them in determining viability of bowel. The lead encasements, Geiger counters, and other necessary paraphernalia might make the method cumbersome, however.

Thus there is need for a simpler, more direct, less cumbersome test for viability of the intestine.

As a rule, tests for viability are employed after various therapeutic measures have been tried to revive the questionable bowel. Therapeutic approaches to the revival of bowel just released from strangulation can be listed as follows: (1) the application of hot packs to the bowel; (2) inhalation of pure oxygen; (3) injections of procaine hydrochloride into the mesentery near the vessels of the segment; (4) the use of heparin to prevent propagation of thrombi and to decrease the viscosity of the blood. Each of these measures carries its own drawbacks.

Hot packs may not only damage the serosal surface and thus lead to adhesions, but they actually enhance thrombosis in the superficial mesenteric veins close to the segment. However, it is well known that mild heat acts as an active vasodilator. Temperatures above 34 degrees C. usually exceed that of normal exposed bowel and can therefore be termed warm. Lewis has shown that temperatures of over 47 degrees C. may cause tissue damage and even thrombosis.

The inhalation of oxygen for purposes of enhancing the recovery of strangulated bowel was introduced by Chase some 20 years ago. It is true that circulating blood takes on a bright red color after oxygen inhalation, and therefore any normal tissue it traverses is similarly affected. However, there is no physio-

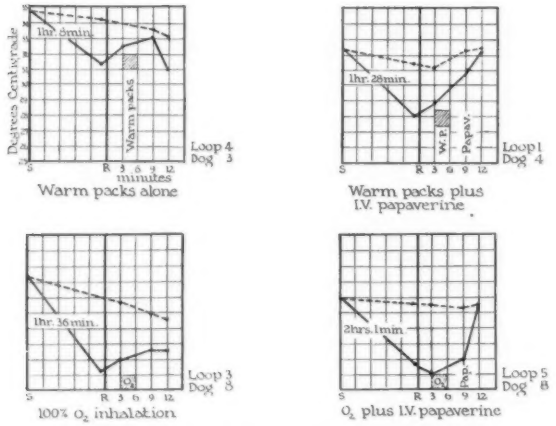


Chart 3. Comparison of typical temperature curves following various forms of resuscitative therapy in venous type strangulations of questionable appearance. Note that the adjunctive use of papaverine apparently enhances the temperature response to the other forms of therapy.

logical evidence available to show that oxygen acts directly on blood vessels. Thus, for oxygen to get into tissues whose vessels are partially closed, it must be used in conjunction with a vasodilating measure.

Injections of procaine hydrochloride into the mesentery were suggested by Herrlin and associates in 1942. They apparently appreciated the vasospastic factor in cases of doubtful circulatory competence of the intestine, and they claimed some of the vasospasm was released as a result of the injections.

The use of heparin is quite logical on the basis of the slowed circulation and the clumping of cells in the spastic vessels. But as we demonstrated in 1942 (20), heparin should not be used in cases of strangulation unless the segment has already been resected. It was shown that heparin increased the degree of hemorrhage into the lumen and intramural structures to such an extent that such animals bled to death, while control animals with similarly released strangulations survived. On the other hand, heparin is very useful in preventing the propagation of thrombi following resection of an infarcted segment. In strangulation, therefore, our efforts at immediate resuscitation cannot utilize anticoagulant therapy and must be directed toward vasodilating measures.

As stated, it may appear paradoxical to employ vasodilating measures in the treatment of a condition in which the vascular bed becomes more and more relaxed as anoxia continues. The answer apparently lies in the difference between the cumulative passive relaxation resulting from anoxia on the one hand, and therapeutic active dilatation in vessels still maintaining a good state of tone (reactivity) on the other.

Our present approach was directed toward the employment of a vasodilating agent whose action was not dependent on the integrity of the nerves. We chose papaverine hydrochloride, a member of the isoquinoline group of opium alkaloids. It apparently acts directly on the smooth muscle cells within the blood vessel wall (7, 25). A rather sizable literature has accumulated on the successful use of papaverine in relieving vasospasm in acute peripheral, coronary, and pulmonary occlusions. Madsen (26) reported 1 case of mesenteric arterial embolism apparently treated successfully with papaverine. This report was interesting from several aspects, although the presence of actual embolism was not proved. The drug has been advocated empirically as adjunctive therapy in mesenteric occlusion, but proof of its value has never been substantiated

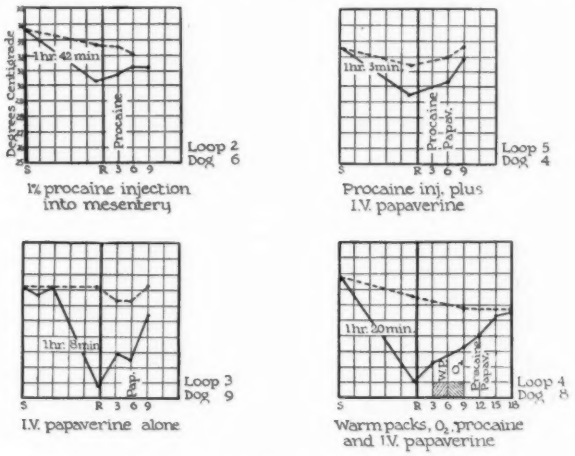


Chart 4. Further comparison of typical temperature curves following various forms of resuscitative therapy. The combined effect of all four therapeutic measures is apparently of greatest value.

by experiment. Some of the evidence on the beneficial effects of this drug in peripheral vascular disease has been equivocal, and in several reports it has been shown to be of no value (24). Apparently the nature of the local pathology and the degree of tone remaining in the blood vessels has much to do with the success or failure of the drug. Furthermore, dosages have never been uniform and its action is relatively short-lived. Experimental studies on the value of papaverine in the resuscitation of strangulated bowel have not been previously reported, to our knowledge.

In preliminary experiments we tested the effects of papaverine by responses in the gross color of strangulated loops. Next, we employed surface temperature readings as a more refined test of its efficacy. Finally the effect of papaverine was studied in comparison with that of well known measures now in use, in order to determine a means of obtaining the maximal response to therapy.

PRELIMINARY EXPERIMENTS ON THE EFFECT OF PAPAVERINE HYDROCHLORIDE ON THE GROSS APPEARANCE OF STRANGULATED INTESTINE

In order to eliminate the question of subjective impressions of color change, color photography was employed. In each experiment two dogs of about equal weight (7 kilos) were anesthetized with intravenous nembutal after a 24 hour starvation period. Every attempt was made to produce precisely the same type of strangulation in each of the 2 dogs. Venous type strangulations were made with binding tape for equal periods of time before release. Among the variables which required standardization were the tightness of the strangulating tape and the anatomical location of the loop. Even in dogs starved for 24 hours, the amount of intestinal contents may vary. To obviate this variable, only those segments which, upon release, appeared identical to their control counterparts were used for testing the effects of papaverine.

Two speed graphic cameras with identical lens corrections were set up under identical lighting conditions and identical exposure factors. One dog served as a control and received no therapy after the strangulations were released, while the other dog received a slow injection of ½ grain[1] of papaverine hydrochlo-

[1] A 1 cubic centimeter ampul of papaverine contains ½ gr. (0.032 gm.) of active principle. This is a relatively large dose, equivalent to .0045 gm. per kilogram. Blood pressure studies in previous experiments using this dose revealed a transient (2-minute) drop in blood pressure and a fleeting stimulation of respiration from which all dogs recovered with no ill-effects. We found that papaverine had a negligible effect on intestinal motility.

ride into the femoral vein 3 minutes after the release of each segment. The strangulations were released at ½ hour intervals, from ½ to 3 hours after initial strangulation. Photographs were taken of the released loop in each dog 3 minutes after papaverine was injected (Figs. 5, 6, 7, frontispiece).

The photographs gave us the impression that papaverine definitely improved the color response of the bowel following strangulation, up to about 1½ hours of strangulation. It must be remembered that in longer loops the time factor is considerably lengthened. After 2 hours of venous type strangulation, no recovery could be seen in either treated or control loops (Fig. 8, frontispiece). Three-inch loops in dogs subjected to venous type strangulations for more than 1½ hours are usually beyond recovery under any circumstances.

SURFACE TEMPERATURE CHANGES IN INTESTINAL LOOPS OF QUESTIONABLE VIABILITY FOLLOWING PAPAVERINE HYDROCHLORIDE AND OTHER RESUSCITATIVE MEASURES

Strangulations of both the venous and arterial types were produced in the manner mentioned previously. The strangulations were left in place for varying periods of time until the loop reached a stage of questionable viability. Surface temperatures were recorded while the strangulation was still in place and compared with a control reading of normal bowel. After release of the strangulation, temperatures were again taken following a lapse of 3 minutes. One group was treated with hot packs for 3 minutes; a second group received an injection of novocain perivascularly into the mesentery; a third group was given inhalations of pure oxygen; and a fourth group received 1 cubic centimeter of papaverine hydrochloride in a peripheral vein by slow injection. The effect of these procedures and various combinations of them on surface temperature was observed. A prediction was made in each case as to the viability of the segment and its accuracy checked by autopsy examination.

COMPARATIVE ANALYSIS OF METHODS OF RESUSCITATION OF STRANGULATED INTESTINE

The number of strangulated loops subjected to the various forms of therapy is small since we chose only those of very questionable viability. Such a study contains many variables and is rather difficult to control for purposes of accurate quantitative comparison. Thus, we were satisfied to determine in a qualitative manner whether a given therapeutic measure caused a favorable response or not.

After the strangulation was released for 3 minutes and the temperature recorded, treatment was instituted and temperatures checked at 3 minute intervals up to 36 minutes in some instances. The forms of treatment included warm packs locally, papaverine hydrochloride intravenously, procaine hydrochloride injections into the mesentery, oxygen inhalations, and various combinations of these measures. Typical temperature responses are shown in Charts 3 and 4.

We found that in most instances, each of these measures has some merit, and there is no reason why all of them should not be employed. However, their effects are not necessarily mathematically cumulative.

VALUE OF PAPAVERINE AS AN ADJUNCTIVE FORM OF THERAPY

In general, we found that the most consistent rises in temperature resulted when papaverine hydrochloride was used in addition to one or several of the other resuscitative measures. For example, when warm packs were applied to the segment after its temperature stabilized, there resulted a temporary rise. Three minutes later, however, there was a decline in temperature. If then papaverine was injected, the temperature rose and held a more or less constant level. Such a loop was considered viable. If the papaverine gave little or no response, the loop was declared nonviable.

Oxygen inhalations alone gave only a moderate response in temperature in 12 loops. Although the color seemed to improve in some cases, it by no means did so in every instance. If the segment was still viable, the intravenous injection of papaverine even 30 minutes after the inhalation of oxygen resulted in a substantial rise in temperature, often equalling that of the adjacent normal bowel.

Perivascular injections of procaine hydrochloride into the mesentery were made in 7 instances. They produced little or no response

when used alone, but when papaverine was injected intravenously, the rise in temperature was definite, provided the loop was recoverable. We could not determine whether this was the combined effect or the effect of papaverine alone, since the response to papaverine varied from case to case.

When papaverine alone was used, the temperature of the loop, if it was recoverable, rose in each of 15 instances. However, in several instances the temperature could be boosted further by adding another measure, such as warm packs. We did not administer the drug postoperatively in any of our animals, although this might be advisable clinically.

ACCURACY OF SURFACE TEMPERATURE AS A TEST OF VIABILITY

Our predictions of viability, based solely on surface temperature responses in over 50 strangulations were correct in every instance but two. These two segments, each in a different animal, were found intussuscepted at postmortem. Our presumption was that after regaining viability, they were restrangulated by intussusception after the abdomen was closed, and had they not intussuscepted they would have survived. We therefore thought of the test as one which might be of some clinical value.

SUMMARY AND CONCLUSIONS

The recovery of strangulated intestine has been investigated from the standpoint of the behavior of the involved vasculature. Evidence obtained by intestinal surface temperature readings indicates that there is considerable residual vasospasm in the minute vessels of a still viable loop. Of the many factors which affect the recoverability of strangulated intestine, vasospasm is of no small significance, whether the strangulation be primarily arterial or venous.

The gross appearance of a still viable arterial type strangulation is markedly different from that of a still viable venous type strangulation. By the time an arterial strangulation assumes the gross appearance of a venous type, its vasculature has lost all reactivity and is beyond recovery. However, an arterial type strangulation retains recoverability more than 5 times as long as does the venous type.

Release of a viable arterial type strangulation results in reactive hyperemia followed by a phase of vasospasm, as demonstrated by intestinal surface temperature readings. Release of a viable venous type strangulation is followed by a slow rise in temperature to the control level or not quite reaching it. This latter phenomenon might conceivably be due to the following, acting separately or in combination: (1) the necessity of the renewed blood flow to move the stagnant venous blood through engorged veins; (2) the formation of thrombi causing a rerouting of circulating blood through fewer channels; (3) arteriolar spasm due to secondary arterial occlusion which may follow venous occlusion; (4) reflex arteriolar spasm following pure venous occlusion.

In nonviable segments of either type, release of the strangulation results in a poor temperature response or an actual decline in temperature. As secondary relaxation of the vasculature progresses during strangulation, there is a loss in reactivity to resuscitative measures.

The response of intestinal surface temperature to the various forms of resuscitative therapy is offered as a simple test for viability which may have some clinical application. The rise in temperature of the affected loop as compared to normal bowel is an indication as to its recoverability.

Papaverine hydrochloride is of value in releasing residual vasospasm, thus aiding the recovery of bowel following strangulation, provided the loop is recoverable. Comparative studies between the effects of warm packs, oxygen inhalations, mesenteric novocain injections, and the intravenous administration of papaverine were attempted. All these measures were found to have some value in increasing the blood flow through a still viable loop of intestine. When papaverine in large doses was given following one or a combination of the first three measures, an additional response was usually seen.

REFERENCES

1. Abramson D. I. Vascular Responses in the Extremities of Man in Health and Disease. Chicago: University of Chicago Press, 1944.
2. Allen, E. V., and Crisler, G. R. J. Clin. Invest., 1937, 16: 649.
3. Allen, E. V., and MacLean, A. R. Proc. Mayo Clin., 1935, 10: 216.

4. Chase, J. Quoted by J. O. Herrlin, S. J. Glasser, and K. Lange (16).
5. Collins, D. C. Am. J. Surg., 1936, 33: 210.
6. Idem. California West. M., 1939, 51: 307.
7. Denk, W. Münch. med. Wschr., 1934, 81: 437.
8. De Takats, G. J. Am. M. Ass., 1936, 106: 1003.
9. De Takats, G., Beck, W. C., and Fenn, G. K. Surgery, 1939, 6: 339.
10. De Takats, G., and Jesser, J. H. J. Am. M. Ass., 1940, 114: 1415.
11. Eichna, L. W., and Wilkins, R. W. Bull. Johns Hopkins Hosp., 1941, 68: 450.
12. Elek, S. R., and Katz, L. N. J. Pharm. Exp. Ther., 1942, 74: 335.
13. Idem. J. Am. M. Ass., 1943, 122: 196.
14. Gosset, A., Bertrand, I., and Patel, J. Ann. anat. path., Par., 1932, 9: 841.
15. Hatfield, C. A., Guyers, R. A., and Walkling, A. A. Surg. Gyn. Obst., 1945, 81: 530.
16. Herrlin, J. O., Jr., Glasser, S. J., and Lange, K. Arch. Surg., 1942, 45: 785.
17. Heymans, C., Bouckaert, J. J., and Dautrebande, L. Arch. internat. pharmacodyn. therap., 1930, 39: 400. Quoted by Kuntz, A. The Autonomic Nervous System. Philadelphia: Lea and Febiger, 1945.
18. Lange, K., and Boyd, L. J. Med. Clin. N. America, 1942, 26: 943.
19. Laufman, H. Occlusion of the Mesenteric Blood Vessels and Associated Phenomena. Thesis. Northwestern University Library, 1942.
20. Idem. Surg. Gyn. Obst., 1942, 74: 479.
21. Laufman, H., and Freed, S. C. Surg. Gyn. Obst., 1943, 77: 605.
22. Lewis, T. The Blood Vessels of the Human Skin and Responses. London: Shaw & Sons, Ltd., 1926.
23. Lindner, E., and Katz, L. N. J. Pharm. Exp. Ther., 1941, 72: 306.
24. Littauer, D., and Wright, I. S. Am. Heart J., 1939, 17: 325.
25. Macht, D. I. Arch. Int. M., 1916, 17: 786.
26. Madsen, L. J. California West. M., 1940, 52: 176.
27. McEachern, C. G., Smith, F. H., and Manning, G. W. Am. Heart J., 1941, 21: 25.
28. McKechnie, R. E., and Allen, E. V. Proc. Mayo Clin., 1935, 10: 678.
29. Mokotoff, R., and Katz, L. N. Am. Heart J., 1945, 30: 215.
30. Mulvihill, D. A., and Harvey, S. C. J. Clin. Invest., 1931, 10: 423.
31. Ochsner, A., and De Bakey, M. Tri-State M. J., 1941, 13: 2654.
32. Parsons, R. J., and McMaster, P. D. J. Exp. M., 1938, 68: 353.
33. Perlow, S., and Block, L. J. Am. M. Ass., 1937, 109: 27.
34. Scott, H. G. Arch. Surg., 1938, 36: 816.
35. Scott, H. G., and Wangensteen, O. H. Proc. Soc. Exp. Biol., N. Y., 1932, 29: 424.
36. Scott, H. G., and Wangensteen, O. H. Proc. Soc. Exp. Biol., N. Y., 1932, 29: 748.
37. Scupham, G. W., De Takats, G., Van Dellen, T. R., and Beck, W. C. Arch. Int. M., 1938, 62: 482.
38. Wangensteen, O. H. Intestinal Obstructions. Springfield, Ill.: Charles C Thomas, 1942.
39. White, J. C. The Autonomic Nervous System, in Christopher, F.: A Textbook of Surgery, 4th ed. Philadelphia: W. B. Saunders Co., 1945.

SURGICAL TREATMENT FOR SYMPTOMS PRODUCED BY CERVICAL RIBS AND THE SCALENUS ANTICUS MUSCLE

ALFRED W. ADSON, M.D., F.A.C.S., Rochester, Minnesota

TWENTY-TWO years of experience in the treatment of symptoms produced by cervical ribs and the scalenus anticus muscle have revealed many interesting facts. Section of the scalenus anticus muscle which I suggested and reported on in 1927, instead of removal of the supernumerary rib, continues to be the operation of choice (1, 2). Occasionally, a portion of a completely formed cervical rib has to be cut away with rongeurs to mobilize thoroughly and relieve all irritation on the brachial plexus, in addition to sectioning of the distal end of the scalenus anticus muscle. Cervicothoracic sympathectomy occasionally has to be performed in conjunction with scalenotomy when vascular and vasomotor symptoms predominate. An anomalous formation of the first rib, with the presence of a cervical rib, requires resection to liberate thoroughly the brachial plexus.

THE VASCULAR TEST

I should like to re-emphasize the importance of the vascular test (3), a maneuver to which other authors have attached my name. The test indicates whether or not the volume of the pulse has been altered, suggesting that the subclavian artery has or has not been compressed. If the subclavian artery has been compressed, there is a strong supposition that the brachial plexus also is irritated whenever the scalenus anticus muscle is placed on tension, the artery being displaced posteriorly against trunks of the plexus. The test consists of having the patient take a long breath, elevate his chin and turn it to the affected side (Fig. 1a and b, Fig. 2a and b). This is done as the patient is seated upright, with his arms resting on his knees. An alteration or obliteration of the radial pulse or change in blood pressure is a pathognomonic sign of a scalenus anticus syndrome. Since I called attention to this phenomenon in 1927, it has been too often overlooked in a surgeon's desire to operate for pain in the shoulder and arm supposedly due to the syndrome.

It has been my experience that little has been accomplished by the scalenotomy procedure for the scalenus anticus syndrome without the presence of cervical ribs or unusually large transverse cervical processes unless the result of the vascular test is positive. The test for muscle tenderness and nerve block advocated by Ochsner, Gage, and DeBakey apparently has proved extremely valuable in the selection of patients for surgery when a syndrome of scalenus anticus is considered.

The vascular test has other diagnostic values, such as determination of the presence or absence of subclavian arterial constriction without symptoms when cervical ribs are identified roentgenologically by accident. If the result of the test is negative, surgical treatment is not indicated and the patient should not be told of the finding. If the result of the test is positive, surgery has to be considered then or later, depending on how much constriction has taken place. If the radial pulse can be obliterated, scalenotomy should be performed at once, since I have observed on several occasions atheromatous thickening in the wall of the subclavian artery under the scalenus muscle where friction existed. In 2 patients of mine the artery ruptured at the site of the atheromatous patch after scalenotomy. In one patient, it occurred 12 days after surgery. The hemorrhage was so extensive that the patient died before I could bring him back to the operating room and ligate the subclavian artery. In the second case it occurred just as I had finished the operation. I promptly exposed and ligated the proximal end of the artery. The entire wall of the vessel was brittle in that portion of the subclavian artery that lies posterior to the scalenus anticus muscle. Fortunately, the patient recovered without

From the Section on Neurosurgery, Mayo Clinic, Rochester, Minnesota.

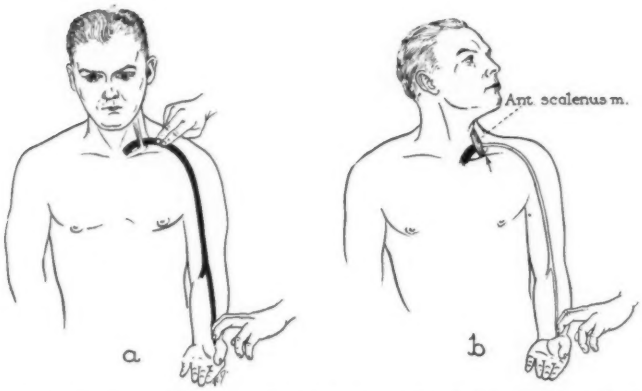


Fig. 1. The vascular test; a, the subclavian and radial arteries identified; b, pulsations of arteries obliterated by inspiration, elevation of patient's chest and rotation of his head to the affected side; in this case, the left.

complications, and was also relieved of symptoms.

TAUT OMOHYOID MUSCLE

The omohyoid muscle in people with long necks not infrequently compresses the brachial plexus and gives rise to paresthesias. Although this muscle usually is divided during the operation, I have purposely left the ends unsutured in several cases. I have done this after an experience with a patient who had undergone scalenotomy elsewhere for the syndrome; this patient also had a small cervical rib. Not being sure that the scalenus anticus muscle had been completely divided, I advised reoperation. I found everything to be satisfactory except that the omohyoid muscle was very tense and acted as a band running diagonally across the brachial plexus. I divided the muscle and closed the wound. The patient was relieved of her symptoms of paresthesia of the lower arm and hand.

DEVELOPMENT OF SUPERNUMERARY RIBS

Jones attributed the embryologic formation of supernumerary ribs to a conflict between forming plexuses and ribs. In higher forms, the limb buds cover several vertebral segments, the nerves from which grow into the buds. However, the diametric growth of the limb buds does not keep pace with the longitudinal growth of the vertebral column, and soon segmental nerves have to pursue an oblique course to enter the buds. Then begins the conflict between the obliquely running nerves and the newly forming ribs. The embryonic nerve trunks are far larger in proportion to the vertebrae and ribs in the embryo than in the fully developed animal. The obliquely running nerves normally impede the growth of the ribs, so discouraging them that they merely form vertebral processes. Todd was of the opinion that the vessels have equal importance with the nerves as causative factors in modification of the upper end of the thorax.

The reported anomalies of the upper end of the thorax run from rudimentary first ribs to double cervical ribs on the same side (5, 24, 25).

Gruber, in 1869, classified cervical ribs. He divided them into four groups according to extent of growth (Figs. 3 and 4): (1) a rib of slight degree, reaching beyond the transverse process; (2) a more advanced rib, reaching beyond the transverse process, either with a free end or touching the first rib; (3) an almost complete rib, the connection with the cartilage of the first rib being formed by means of a distinct band or by the end of the long body of the cervical rib; and (4) a complete rib, possessed of a true cartilage which unites with the cartilage of the first rib (Fig. 5).

"The surgical anatomy of cervical rib is essentially that of the posterior triangle of the

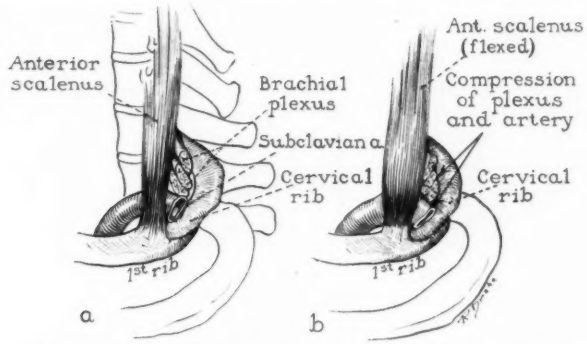


Fig. 2. The vascular test; a, appearance of the anatomic structures when the scalenus anticus muscle is relaxed; b, constriction of the subclavian artery and brachial plexus when the scalenus anticus muscle is contracted.

neck. The posterior triangle curves obliquely around the lateral aspect of the neck. It is bound in front by the sternomastoid, behind by the trapezius, while its base is formed by the middle third of the clavicle. Its floor is formed from above downward by the splenius capitis, levator scapulae, scalenus medius, and posticus muscles, the first rib and the first digitation of the serratus magnus. The scalenus anticus muscle does not form a part of the posterior triangle since it is directly behind the clavicular portion of the sternomastoid muscle" (31).

Todd (47–49) believed that the scalenus and intercostal muscles arise from the same muscle plane, forming two sheets, the outer forming the scalenus anticus and minimus muscles; the inner, the scalenus medius and posticus muscles. These sheets of muscles are continued as the internal and external intercostal muscles. The subdivisions of the scalenus muscles are made by the passage of vessels and nerves. The course of the subclavian artery through the scalenus muscles corresponds to that of an intercostal artery through the wall of the thorax.

The contents of the posterior triangle are: (1) arteries—the third part of the subclavian, the transverse cervical and suprascapular; (2) veins—the subclavian and external jugular; and (3) nerves—the brachial plexus.

The subclavian artery is divided into three parts by the scalenus anticus muscle. The first part is medial to the muscle, the second part directly behind, and the third part is lateral. The subclavian vein is below and in front of its artery with the scalenus anticus muscle lying between. The phrenic nerve passes downward in front of the scalenus anticus muscle toward the medial border. The cervical pleura is directly below and behind the first and second parts of the subclavian artery. It extends higher in the neck in the case of persons with cervical rib. An important relationship to the first part of the subclavian artery on the left side is the thoracic duct which arches down in front of it in order to end at the junction of the internal jugular and subclavian veins. The first rib is below the third part of the subclavian artery.

INCIDENCE OF SUPERNUMERARY RIBS

To determine the incidence of cervical ribs, a study was made of roentgenologic findings in a complete series of patients registered at the Mayo Clinic between given dates. The study was made before 1927, when fewer roentgenograms were made of the cervicothoracic portion of the spinal column than are made today. The study showed that 303 patients had cervical ribs, an incidence of 0.0563 per cent, or 5.6 patients per thousand. Of these 303 patients, 84 were males and 219 were females. Roentgen-ray examination revealed bilateral cervical ribs in 143, a cervical rib on the right side in 70 and a cervical rib on the left side in

90 cases. In cases of unilateral cervical rib, there frequently existed on the opposite side a supernumerary costal tubercle which did not extend beyond the transverse process of the cervical vertebra and was, therefore, not classified as a cervical rib; it might easily have been placed in Gruber's first class. In 167 cases of the group of 303, the presence of cervical ribs was discovered accidentally because there were no symptoms (19). Thus, 55 per cent of the patients were symptom free. Of the remaining 136 patients, only 36 were operated on before 1928 (23); among the others the symptoms were mild or too indefinite to justify surgical treatment. However, in view of the added information now obtainable by the vascular test and in view of the observations I have made while performing scalenotomy subsequently, I suspect that a larger percentage of patients should have had surgical treatment.

White and associates, in a study of congenital malformations of the first thoracic rib, revealed some interesting data concerning the incidence of malformations and the similarity between the symptoms of malformations and those resulting from cervical ribs. He quoted Haven, who reviewed 5,000 routine roentgenograms of the thorax in which he found 38 abnormalities of the first thoracic ribs as compared with 37 cervical ribs. His findings of cervical ribs represented an incidence of 0.074 per cent or 7.4 persons with cervical ribs per 1,000 (7, 9, 13, 40). These figures slightly exceeded ours.

ETIOLOGIC FACTORS

Authors attempting to explain the mechanism responsible for the symptoms associated with cervical ribs or for the symptoms developing without the presence of cervical ribs have contributed numerous reports of cases, with peculiarities in this or that case.

There are several factors that play important rôles in the production of the symptoms. Probably no one factor is responsible for all the symptoms, although some are more responsible than others. It is difficult to explain why all patients with completely formed cervical ribs do not have symptoms. It is just as difficult to explain why symptoms develop in so few of these cases when it is considered that the shoulder girdle has a tendency to descend as all people become older. There must be a good reason why the symptoms develop in early adult life and rarely in childhood. It is not so difficult to understand why vascular phenomena and vasomotor disturbances arise, other than the fusiform aneurysm which only rarely develops in the third portion of the subclavian artery lateral to the outer border of the scalenus anticus muscle.

I believe there are three factors responsible for the symptoms, with the scalenus anticus muscle being the chief one. The first factor is that those persons in whom symptoms develop have an anatomic structure of the neck which is different from that of normal persons. The cervical portion of the spinal column is longer, and this same congenital defect accounts for the high-lying second division of the subclavian artery. The base of the posterior cervical triangle which runs parallel with the superior border of the clavicle is shortened. The width of the base, and the distance between the posterior surfaces, of the scalenus anticus and the scalenus medius and posticus muscles likewise are congenitally shorter, or perhaps it should be called lower, so that the space through which the subclavian artery and the cords of the brachial plexus must pass is decreased. Then, if there is present a cervical rib or a large cervical transverse vertebral process, the structures passing through the base of the triangle are still further compressed, since the bony structures elevate the floor and displace the plexus forward against the subclavian artery. The subclavian artery is unable to dislodge itself and, therefore, is caught, compressed, and irritated between the brachial plexus from behind and the scalenus anticus muscle in front.

I have also observed that in cases in which circulatory disturbances and brachial symptoms are associated and are severe, the insertion of the scalenus anticus muscle invariably is wide, the muscle being reflected laterally beyond the operculum of the first rib. This narrows the space between the lateral border of the scalenus anticus muscle and the cervical rib, and accounts for additional compression of the brachial plexus and the subclavian artery.

The second factor, which is concerned more with the onset of symptoms, probably is associated with the descent of the shoulder girdle (6). This process begins in early adult life. The descent or sagging of the shoulders possibly could add sufficient traction on the brachial cords to precipitate symptoms when the congenital abnormality of the lower part of the neck had already reduced the normal freedom of movement.

I wish to report a number of observations to support my opinion that the scalenus anticus muscle, the third and chief factor, was the one chiefly responsible for the symptoms (10, 37, 42).

My attention was called to the possible rôle the scalenus anticus muscle played in the cervical rib syndrome on June 13, 1925, when I was asked to examine a patient who had gangrene of the first and second fingers of his right hand. It was known that he had a cervical rib on the right side, but we were unable to explain the unilateral vascular changes in the fingers. The brachial, radial, and ulnar arteries had no pulsations. The right hand and lower part of the arm were cyanotic, cold and moist. In view of my interest in vasomotor disturbances, I advised surgical exploration of the cervical rib. This was done. I used the anterior approach that I still use —the one in which the base of the posterior cervical triangle is explored through a unilateral collar-skin incision. After reflecting the clavicular portion of the sternocleidomastoid muscle, I exposed the scalenus anticus muscle.

Fig. 3. A completely formed right cervical rib which is producing symptoms, and an incompletely formed cervical rib on the left which is not producing symptoms.

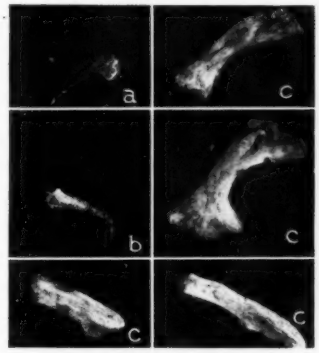


Fig. 4. Surgical specimens of cervical ribs, illustrating the different sizes and shapes under Gruber's classification: a, group 2; b, group 3; c, group 4.

The muscle was in my way as I explored the cervical rib, so I proceeded to section the costal attachment. I noticed that with each inspiration of the patient the scalenus anticus muscle bulged and became tense and completely collapsed the subclavian artery. After I had divided the muscle, there remained an indentation where the muscle had rubbed the artery. This indented portion of the artery was shell-like to palpation, for a calcareous atheroma had developed there. The vessel did not give way at the site of this atheroma, as it did in the 2 other cases to which I have referred.

After sectioning the scalenus anticus muscle, I continued the dissection. I was impressed by the damage that had been done to the artery. When the artery was released from the pressure of the muscle, it began to slip back into the thorax, and as it did so it released the brachial plexus. Hence, the brachial plexus no longer was jammed over against the cervical rib. It was apparent that removal of the cervical rib would have been insufficient to relieve the constriction of the subclavian artery. It likewise was apparent that sectioning of the scalenus anticus muscle, which promptly contracted upward, relieved the situation and would have done so without removal of the cervical rib. However, I proceeded to remove the cervical rib by the anterior approach, since in all surgical teaching up to that time removal of cervical ribs had been the practice advocated.

After having several similar experiences, I became convinced that it was not necessary to remove cervical ribs routinely, and that the chief etiologic element was the scalenus anticus muscle. This point was further substantiated by experience with the vascular test. During the operation I could increase the tension on the scalenus anticus muscle by having the anesthetist elevate the patient's chin and rotate the head to the affected side. The increased tension increased the pressure and further collapsed the subclavian artery with each inspiration. It was also observed in employment of the test preoperatively that the more completely the circulation was obliterated at the wrist, the greater was the evidence of arterial compression when the subclavian artery was exposed during the operative procedure.

The explanations vary somewhat as to why the symptoms begin in early adult life. Descent of the shoulder girdle may be one of the contributing factors. I have always held that this process occurred at the height of muscular development, which would explain the hypertrophy of the scalenus anticus muscle. Although both of these factors—descent of the shoulder girdle and hypertrophy of the scalenus anticus muscle—may contribute to the mechanism, I have never been called on to operate on athletes, wrestlers, boxers or football players with marked muscular hypertrophy or with heavy descending shoulders. Perhaps the person who has these congenital anomalies learned early in life that it was painful to pursue vigorous activity and therefore avoided athletics.

We still have failed to explain why the scalenus anticus muscle has hypertrophied in so many cases. It is possible that the muscle, with other accessory respiratory muscles, is called on to lift a heavier load during respiration in adult persons than in children because the shoulders and pectoral girdle have increased in weight.

I believe the scalenus anticus syndrome which develops with or without cervical ribs results from a combination of factors. First, the congenital anomaly restricts the activity and freedom of movement of the brachial plexus and the subclavian artery. As long as no activating factor is introduced, the artery may be compressed slightly with each inspiration without the production of symptoms. But as the load on the scalenus anticus muscle is increased the artery is compressed and displaced backward, jamming the plexus against the floor, the cervical rib or the transverse process of the cervical vertebra. All this varies in degree, depending on the room within the base of the posterior triangle of the neck. The neurologic symptoms depend on the nerve trunk involved and the degree of pressure applied. The atheromatous changes of the subclavian artery, with resulting thrombosis and occlusion, no doubt are due to local damage and a liberated embolus. The degree of damage bears a direct relationship to the trauma. The presence of adhesions about the subclavian artery suggests thrombosis of the vasa vasorum and an inflammatory reaction. The tenderness of the scalenus anticus muscle that Gage has brought to our attention probably is caused by thrombosis of arterioles from pressure trauma within the muscle. It undoubtedly gives rise to a local inflammatory process and sensations of pain which Gage said he could temporarily relieve with a local anesthetic agent.

The vasomotor phenomenon results from stimulation of the fibers as they pass, intermingled with the myelinated nerve fibers of the brachial trunks. In the patients who present an unusual vasomotor disturbance, the sympathetic nerve distribution probably is as Telford and Stopford suggest. They, in reviewing a number of dissecting-room subjects without cervical rib, found that the lower trunk of the brachial plexus in 8 cadavers lay on the upper surface of the first rib. In the eighth cadaver, they found that in the inferior part of the lower trunk of the brachial plexus there was a distinct and separate bunch of unmyelinated fibers which they interpreted as being sympathetic fibers passing to the upper limb by the way of the lower trunk, and which had not yet become incorporated with and intermingled among the other fibers of the lower trunk. The fusion of the sympathetic fibers with the lower trunk was, in this instance, at a more distal point than usual. It is my impression that a similar situation occurs now and

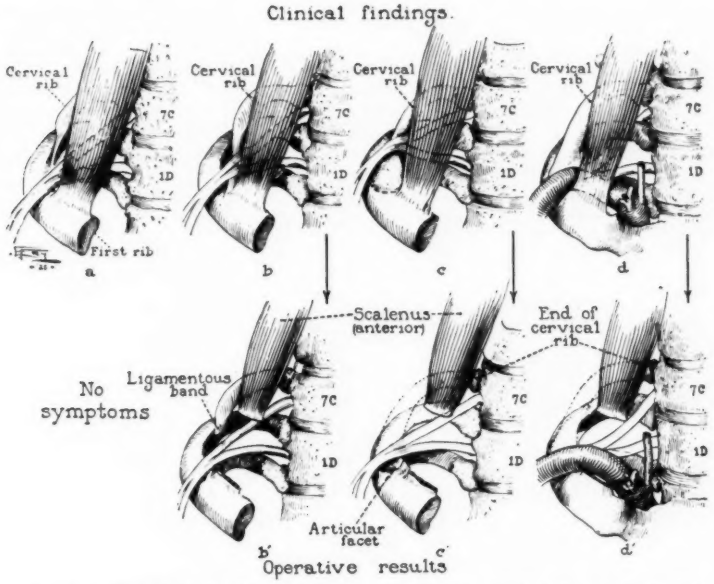


Fig. 5. a, A cervical rib with a fibrous band between the cervical rib and the thoracic rib; such a cervical rib does not produce symptoms because there is ample space between the lateral border of the scalenus anticus muscle and the ligamentous band of the cervical rib; b, compression of the lower trunk of the brachial plexus by pressure of the scalenus anticus muscle against the fibrous band; b′, relief of compression obtained by tenotomy of the scalenus anticus muscle and division of the fibrous band; c, compression of the lower trunk of the brachial plexus by pressure of the scalenus anticus muscle against the completely formed cervical rib; c′, relief of compression obtained by either tenotomy of the muscle or resection of the rib; d, compression of the lower trunk of the brachial plexus and the subclavian artery against the completely formed cervical rib; d′, relief of compression achieved by tenotomy of the scalenus anticus muscle or by resection of the cervical rib.

then when cervical ribs are present because the vasomotor symptoms of vasospasm and hyperhidrosis predominate and are out of proportion to other neurologic findings, so that major involvement of postganglionic sympathetic fibers is suggested.

Telford and Stopford (44) further wrote that in the presence of a cervical rib, the cervical sympathetic fibers are more likely to be irritated than would be true if the rib were not present. This point is substantiated in that the vasomotor phenomena are less marked in the scalenus anticus syndrome when cervical ribs are absent than when they are present.

In discussing the influence of irritation of the sympathetic nerves Telford and Stopford said it is their opinion that the irritation produces enough spasm of the vasa vasorum to result in constriction and obliteration of the vessels, with resulting nutritional changes in the larger arterial walls which ultimately might lead to thrombosis. I presume it is possible that this process of thrombosis of the vasa vasorum and impairment of the arterial wall may account for the development of the fusiform aneurysm in the third portion of the subclavian artery lateral to the scalenus anticus muscle. It is a common occurrence to see that the third portion of the subclavian artery is much larger in diameter than the first portion, which is medial to the scalenus anticus muscle. I have always attributed this to paralysis of the vasomotor fibers supplying the third portion of the subclavian artery.

Before proceeding with an enumeration of the symptoms produced by the factors re-

TABLE I.—INCIDENCE ACCORDING TO AGE: 142 PATIENTS WITH SYMPTOMS OF CERVICAL RIB OR THE SCALENUS ANTICUS SYNDROME

Age, years*	Group			Totals
	A	B	C	
10 to 20	3	0	0	3
20 to 30	13	11	5	29
30 to 40	18	7	18	43
40 to 50	17	5	10	32
50 to 60	12	3	5	20
63			1	1
Totals	63	26	39†	128†

*Youngest, 14 years; oldest, 63 years.
†The age of the patient at the time of onset of symptoms could not be earned in all cases.

sponsible for the scalenus anticus syndrome, I should like to present a word of caution and suggest that clinicians and surgeons consider other causes for pain in the shoulders, arms, and neck. I agree with Ochsner and associates, Eaton and McGowan, who have emphasized that numerous conditions may produce pains about the shoulders, neck, arms, and hands. The more common ones are bursitis, cervical arthritis, myositis, fibrositis, brachial neuritis, Raynaud's disease, thromboangiitis, neoplasms within the spinal canal, neoplasms of the peripheral nerves and protruded intervertebral disks. In addition to all these, there are added the functional elements —exemplified by the patient who complains of pain "here and there," which includes the shoulders, neck, head and even the arms at some time or other. I presume that it is needless to emphasize the importance of a careful study and an accurate differential diagnosis. It is certain that scalenotomy will not relieve the symptoms which are produced by the lesions just mentioned.

SYMPTOMS

The symptoms vary according to the structure chiefly involved (45, 46, 50, 51, 53). Pain is the most common symptom. Often a pulsating mass can be detected above the clavicle; a bruit may be elicited in the same area. Paresthesia and anesthesia are not uncommon. Paralysis occurs less frequently, as does gangrene of the finger tips. Symptoms of vasomotor disturbances appear rather frequently. One hand is cooler, more sweaty and dusky, although not truly cyanotic, than the other hand when the condition is unilateral (22, 35).

Onset of symptoms. Cervical ribs have been recognized in children (41) by the presence of a tumor in the neck. Murphy and Donaldson thought the most common age of the patient was from 12 to 18 years. Beck thought the symptoms were first manifested after the patient had reached the age of 20 years; Evans believed they appeared between the ages of 20 and 30 years. The youngest patient in the present Mayo Clinic series was 14 years old and the oldest was 63 years (Table I).

The pain may be sharp and lancinating or a dull ache. It usually courses downward over the ulnar and median nerves, but occasionally extends upward to the shoulder and into the neck. The pain may be more or less continuous, but invariably it is exaggerated by rotation of the patient's head or a forceful downward pull of the shoulder. If patients have been told that they have cervical ribs, they are likely to complain of vague pains and general discomfort about the neck and shoulders which I doubt can be attributed to the existence of short cervical ribs. The patient with cervical ribs that actually produce symptoms usually gives the history of pain which follows any sudden or violent exertion. Housewives usually complain of extending pain after sweeping, washing, or dusting. One woman complained of pain and numbness along the distribution of the ulnar nerve after difficult labor. A physician complained of severe pain that extended along the median and ulnar nerves after he had struggled with an insane patient who attempted to commit suicide. Hyperesthesia, paresthesia, and anesthesia may be associated with the pains and may persist after strenuous exertion. Atrophy of the muscles supplied by the brachial plexus occurs infrequently; when it does occur, it is manifested late in the course of the disease and is rarely complete.

Vascular symptoms may be ranged in three categories. The first are those which result from changes in blood flow, the blood flow being altered by varying degrees of constriction of the subclavian artery. Patients will com-

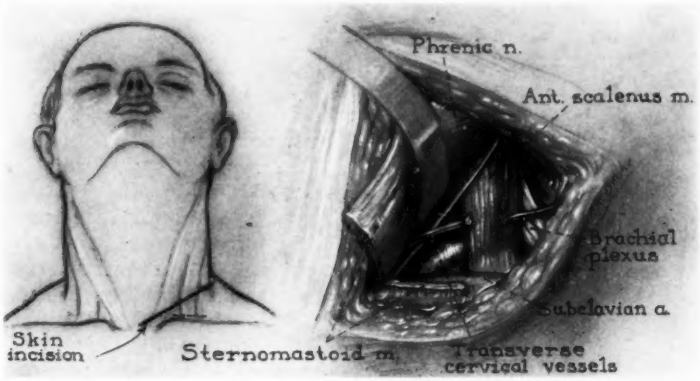


Fig. 6. The operative incision and the anatomic structures in the posterior triangle of the neck.

plain of not being able to work with their hands raised above their shoulders, of not being able to drive a car, to lift a heavy object, or to sleep on their sides because one or more fingers become numb when they attempt such things.

The second group of vascular symptoms are caused by actual organic changes (22, 35) in the subclavian artery and its terminal branches, characterized by occlusion of the radial, ulnar, and brachial arteries, and the appearance of edema, cyanosis, and gangrene of one or more fingers.

The third group of vascular symptoms are caused by disturbances of the sympathetic nervous system (43), characterized by vasomotor changes not unlike those observed in Raynaud's disease (39). The skin covering the hand is more likely to remain cool, dusky, and moist rather than to pass through color changes such as occur in Raynaud's disease. Horner's syndrome on the affected side has been observed many times.

The scalenus anticus syndrome, without the presence of a cervical rib, has been established as an independent entity. Naffziger and Grant, Ochsner, Gage and DeBakey, Jelsma, Love, and others have ably described the syndrome and have supported their opinions by reports of cases. The only additional comment I can make is to emphasize the importance of an accurate diagnosis if relief is to be expected from scalenotomy.

SURGICAL TREATMENT

A collar incision (1–3) is made for a distance of about 5 centimeters, extending upward and backward from the sternoclavicular articulation over the posterior triangle. The dissection is carried through the platysma myoides muscle and fat until the tendon of the sternocleidomastoid muscle, with its attachment to the clavicle, is exposed. The clavicular attachment is divided between two forceps. The muscle portion is then reflected mesially, so that the tendon of the omohyoid is exposed. This tendon is divided, and the tendinous attachment of the scalenus anticus muscle, with the phrenic nerve running obliquely across it from the lateral to the mesial border is exposed (Fig. 6). During dissection, the transverse cervical and the suprascapular arteries are divided and ligated. The scalenus anticus muscle is dissected free, and the phrenic nerve is retracted mesially before the tendinous and muscular insertion is divided. The subclavian artery will appear on the lateral side of the scalenus anticus muscle and, if the space between the cervical rib (or the cervical rib and the tendinous bands to the thoracic rib) and the lateral border of the scalenus anticus muscle is narrow, the surgeon immediately observes compression of the subclavian artery against the trunks of the brachial plexus. On the mesial side of the scalenus anticus muscle the pleura may be observed and, if dissection is carried still farther mesially, the carotid sheath and the vertebral

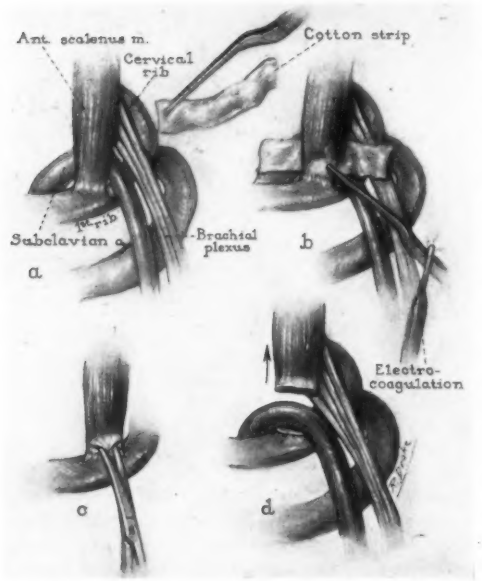


Fig. 7. Steps in the surgical procedure and in protection of the subclavian artery during operation; a, insertion of a strip of cotton between the subclavian artery and the scalenus anticus muscle; b, use of electrocoagulation to control bleeding while the tendinous muscular attachment of the scalenus anticus muscle is being sectioned; c, sectioning of the musculotendinous insertion of the scalenus anticus muscle with scissors; d, when the scalenus anticus muscle has been sectioned, the subclavian artery slides forward and assumes normal caliber, and the lower trunk of the brachial plexus likewise slides forward and downward.

artery will be exposed; this, however, is unnecessary.

It is important to carry the dissection upward on the anterior surface of the scalenus anticus muscle for a distance of 5 centimeters in order to expose the phrenic nerve thoroughly before it is retracted mesially. The surgeon must bear in mind, before he divides the scalenus anticus muscle at its insertion, that it lies over the compressed portion of the subclavian artery, and that the pleura is situated mesially to the inner border of the muscle, in order to avoid injury to both structures. Sectioning of the musculotendinous insertion is most easily accomplished by sectioning the fibers in small groups with scissors (Fig. 7). The cut fibers promptly retract upward, thus exposing the undivided fibers and the compression of the artery. As soon as the scalenus anticus muscle has been divided, the subclavian artery will be seen to slide downward and take on its normal caliber, and the lower trunk of the brachial plexus likewise will slide forward and downward. In the event that there are adhesions between the artery and the brachial plexus, gentle dissestion will be necessary to liberate both. Care is required to avoid injury to the vasa vasorum, for if they are injured, extravasation of blood will take place between the muscular and adventitious coats of the subclavian artery.

Before the surgeon proceeds with sectioning of the bundles of muscle fibers of the scalenus muscle, it is advisable to separate the muscle from the subclavian artery and protect it during the operation by slipping a strip of cotton between the two. This will permit the surgeon to use the electrocoagulating current to control the bleeding while he is sectioning the tendinous muscular attachment of the scalenus anticus muscle. If the muscle is hypertrophied and bulky, it is advisable to resect 3 to 5 centimeters off the lower free end. The incision should be made diagonally across the muscle to avoid a postoperative lump in the neck.

Craig and his assistant in 1937 emphasized the necessity of resection of a portion of the cervical rib, in addition to performance of scalenotomy (15–17). Partial removal of the cervical rib is indicated when the rib is completely formed and occupies a high position as it turns downward (Fig. 8a and b), compelling the lower trunk of the brachial plexus to ride up over it before it continues its course. I remove this portion with a rongeur, exposing the amount I wish to remove by retracting gently the lower trunk of the plexus downward and the middle trunk upward (Fig. 9). If it is necessary to operate on both sides, I do not hesitate to do so during the same operation, and I have not found any contraindications to such a procedure.

Before closing the wound, I reflect a flap of fat between the brachial plexus and the subclavian artery to minimize adhesions and scarring. The wound is closed in much the same manner as any operative wound is closed. The scalenus muscle retracts upward. If division of the omohyoid tendon has been necessary, it

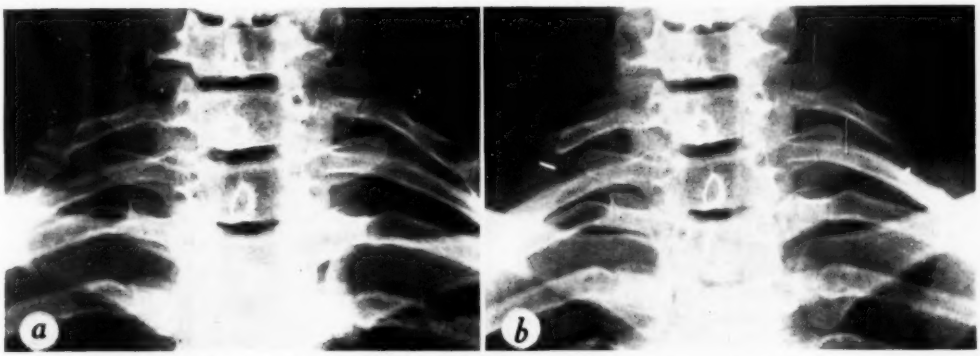


Fig. 8. a, Bilateral cervical ribs, completely formed with articulated extensions; b, results of resection of these ribs in addition to bilateral performance of scalenotomy.

usually is reunited by suture before the clavicular portion of the sternocleidomastoid muscle is resutured with mattress sutures of chromic catgut. The patient may be permitted to sit up on the day after operation; he may be dismissed from the hospital after 3 days and from the surgeon's care as soon as the wound in the skin has healed.

When the technique of the anterior approach and division of the scalenus anticus muscle is compared with the former lateral approach and resection of a cervical rib, the advantages of the anterior approach are readily appreciated, to say nothing of the relative effectiveness of the procedure. The anterior approach can be carried out with ease and without danger of traumatizing the brachial plexus, whereas the latter requires considerable dissection and retraction of the brachial plexus.

REVIEW OF SCALENOTOMY, 1925 TO 1946

The review includes the patients for whom scalenotomy has been performed at the Mayo Clinic during a period of 22 years, from January, 1925, to December, 1946, by members of the neurosurgical staff. There are 142 patients in the series. They have been divided into three groups A, B and C, for comparison of the incidence according to sex and age, marital status, sides involved, occupations, groups of symptoms and results (Tables I, II, III, IV, and V). In group B, some members of which underwent combined operations of scalenotomy and resection of cervical ribs, 9 patients were operated on during 1925 and 1926, when I was convincing myself that scalenotomy could be substituted for resection of cervical ribs in most of the cases. Thus there remain 17 patients for whom, since 1927, it was believed that the combined operation was indicated.

Group A includes patients for whom scalenotomy was performed without resection of cervical ribs (63 patients). Group B includes patients for whom combined operations were performed; that is, scalenotomy and resection of cervical ribs by the anterior approach (26 patients). Group C includes patients for

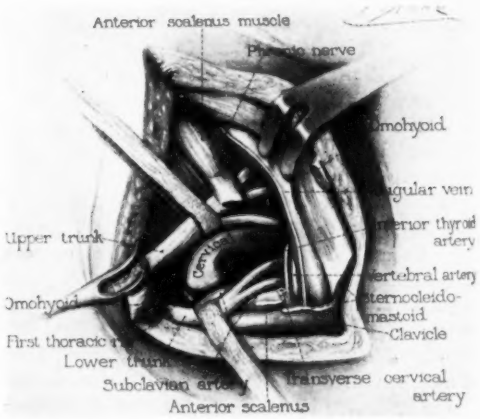


Fig. 9. The anterior approach to the cervical rib when resection is advisable.

TABLE II.—AGE, MARITAL STATUS AND SIDE INVOLVED: 142 PATIENTS (49 MALES AND 93 FEMALES) WITH SYMPTOMS OF CERVICAL RIB OR THE SCALENUS ANTICUS SYNDROME

Data	Group						Totals
	A		B		C		
	Male	Female	Male	Female	Male	Female	
Patients	18	45	5	21	26	27	142
Single	6	15	2	9	9	10	51
Married	12	29	3	10	16	17	87
Widow or widower	0	1	0	2	1	0	4
Right side	4	13	2	8	6	6	39
Left side	8	10	2	7	11	11	49
Both sides	6	22	1	6	9	10	54

TABLE III.—OCCUPATIONS 142 PATIENTS WHO HAD SYMPTOMS OF CERVICAL RIB AND THE SCALENUS ANTICUS SYNDROME

Group	White collar worker	Laborer	Housewife	Totals
A	25	9	29	63
B	11	5	10	26
C	15	19	19	53
Totals	51	33	58	142

TABLE IV.—OCCURRENCE OF SYMPTOMS OF CERVICAL RIBS AND THE SCALENUS ANTICUS SYNDROME AMONG 142 PATIENTS WHO UNDERWENT SCALENOTOMY

Symptoms	Occurrence in group, times			Total
	A*	B†	C‡	
Pain	63	26	44	133
Paresthesia	35	23	39	97
Motor or sensory loss	13	10	4	27
Vascular disturbance	33	10	9	52

*63 patients in this group.
†26 patients in this group.
‡53 patients in this group.

TABLE V.—PERCENTILE REPORT OF RESULTS OF SURGICAL TREATMENT OF 142 PATIENTS WITH SYMPTOMS OF CERVICAL RIB OR SCALENUS ANTICUS SYNDROME

Results	Per cent of group		
	A*	B†	C‡
Relief of symptoms	54	53.8	37.5
Great improvement	36	26.9	43.75
Slight improvement	10	11.5	6.25
Failure		3.8	12.5
Death, 1 case		3.8	

*63 patients in this group.
†26 patients in this group.
‡53 patients in this group.

whom scalenotomy was performed in the absence of cervical ribs (53 patients).

It is rather difficult to give a comprehensive picture of the symptoms of the scalenus anticus syndrome, whether it be associated with the presence or the absence of cervical ribs, since in one case the paresthesias and vascular phenomena may be more prominent whereas in another case the pain which is exaggerated by certain movements may be the only symptom present.

Pain in one form or another is the most common symptom, followed in order of frequency of occurrence by paresthesias, vascular disturbances, and motor or sensory loss. Unilateral vasomotor changes occurred in more than a third of the patients. In 7 patients the vasomotor changes had to be distinguished from those which characterize Raynaud's disease. Two patients had undergone amputation of the index finger. Four patients presented gangrene in the first and second fingers of one hand. The radial pulse was absent in 11 patients.

In group C, in which cervical ribs were absent, the transverse process of the seventh cervical vertebra was unusually large in 16 cases. In the same group the scalenus anticus muscle appeared to be more hypertrophied and more often contained fibrotic bands, than was true in those cases in which cervical ribs were present.

Surgical observations. In all cases in which the result of the vascular test was positive, the scalenus anticus muscle produced a compression of the subclavian artery on each inspiration. Atheromatous plaques with deformities of the subclavian artery were present in 8 cases. In 2 cases the vessel gave way at the sites of these plaques and rupture occurred, as previously reported herein. One of these patients succumbed before ligation of the first

division of the subclavian artery could be effected; the other recovered without complications. Many patients had a fusiform enlargement of the subclavian artery in its third portion lateral to the scalenus anticus muscle, but only one patient had an aneurysm (28, 30, 38). Four patients had anomalous high-arched first thoracic ribs.

The surgical results were both satisfactory and disappointing (Table V). In groups A and B, approximately 54 per cent of the patients were relieved of all their symptoms. Approximately a third were greatly improved. They were able to return to their vocations and to carry on, but were annoyed by twinges of pain during certain movements. These recurrent symptoms were in all probability caused by adhesions in the surgical wound (21). Results of secondary surgical exploration verified this opinion. One patient did not obtain relief by scalenotomy, but secured complete relief after a secondary operation in which the omohyoid muscle was divided and flaps of living fat were used to cover the trunks of the brachial plexus. In 4 other patients the omohyoid muscle was divided at the time scalenotomy was performed. For 5 patients unilaterial cervicothoracic sympathectomy was performed in conjunction with scalenotomy. For 4 patients thyroidectomy was performed at the same time that the scalenotomy was done.

In review of the table concerned with results (Table V), it is apparent that the results in group C, which includes those patients for whom scalenotomy was performed in the absence of a cervical rib, were not so satisfactory as the results obtained in groups A and B. Slightly more than a third of the patients in group C were relieved of their symptoms; many were improved by surgical treatment, whereas for others the treatment accomplished little or nothing. The reason for this, I believe, is too liberal selection of patients for surgical treatment and disregard for the vascular test. Too often the neurosurgeon has been prevailed on to do something when other measures have failed. Perhaps the physician interested in psychosomatic therapy should be called more often in consultation in this particular group of patients. The surgical results bear a direct relationship to the pathologic anatomy.

CONCLUSIONS

Scalenotomy and sectioning of the insertion of the scalenus anticus muscle, occasionally with resection of the distal portion of the muscle when the muscle is markedly hypertrophied, appear to constitute the operation of choice for the condition under consideration.

A combined operation, meaning scalenotomy and resection of cervical ribs, is indicated when the cervical rib is completely formed and is situated high in the neck, so that the brachial plexus must ride over the rib in its course into the axilla. Subtotal resection of the cervical rib can be accomplished with the use of a rongeur, through the same wound, by separation of the middle and lower trunks of the brachial plexus.

REFERENCES

1. Adson, A. W. Atlantic M. J., 1928, 31: 222–232.
2. Idem. Texas J. M., 1933, 28: 739–747.
3. Adson, A. W., and Coffey, J. R. Ann. Surg., 1927, 85: 839–857.
4. Beck, Carl. Fortsch. Röntgenstrahl., 1904–1905, 8: 43–47; (Translation) J. Am. M. Ass., 1905, 44: 1913–1915.
5. Blair, D. M., Davies, F., and McKissock, W. Brit. J. Surg., 1935, 22: 406–414.
6. Boland, E. R. Brit. M. J., 1933, 2: 1068–1069.
7. Brickner, W. M., and Milch, Henry. Surg. Gyn. Obst., 1925, 40: 38–44.
8. Craig, W. McK., and Knepper, P. A. Ann. Surg., 1937, 105: 556–563.
9. d'Abreu, A. L. Brit. J. Surg., 1943, 31: 185–187.
10. Donald, J. M., and Morton, B. F. Ann. Surg., 1940, 111: 709–723.
11. Donaldson, Robert. Brit. M. J., 1909, 2: 931–932.
12. Eaton, L. M. Surg. Clin. N. America, 1946, 26: 810–820.
13. Eden, K. C. Brit. J. Surg., 1939, 27: 111–139.
14. Evans, E. S. J. Am. M. Ass., 1912, 58: 1111–1112.
15. Fischer, Georg. Deut. Zschr. Chir., 1892, 33: 52–56.
16. Flint, E. R. Brit. J. Surg., 1937, 24: 622–624.
17. Funston, R. V. J. Am. M. Ass., 1932, 98: 697–699.
18. Gage, Mims. Surgery, 1939, 5: 590–601.
19. Gladstone, R. J., and Wakeley, C. P. G. J. Anat., Lond., 1932, 66: 334–370.
20. Gruber, W. Ueber die Halsrippen des Menschen mit vergleichend-anatomischen Bemerkungen. St. Petersburg, 1869.
21. Hansson, K. G. Arch. Phys. Ther., 1941, 22: 662–666.
22. Haven, Hale. Yale J. Biol., 1939, 11: 443–448.
23. Henderson, M. S. Am. J. Orthop. Surg., 1914, 11: 408–430.
24. Holling, H. E. Guy's Hosp. Rep., Lond., 1939, 89: 285–295.
25. Hoobler, S. W. N. England J. M., 1942, 226: 942–944.
26. Jelsma, Franklin. Kentucky M. J., 1941, 39: 48–51.

27. Jones, F. W. Proc. R. Soc., Lond., 1913, 6 (pt. 1): 95–113.
28. Lindskog, G. E., and Howes, E. L. Arch. Surg., 1937, 34: 310–319.
29. Love, J. G. Proc. Mayo Clin., 1945, 20: 65–70.
30. MacFee, W. F. Ann. Surg., 1940, 111: 549–553.
31. McGowan, J. M. Ann. Surg., 1946, 124: 71–89.
32. Murphy, J. B. Ann. Surg., 1905, 41: 399–406.
33. Idem. Surg. Gyn. Obst., 1906, 3: 514–520.
34. Naffziger, H. C., and Grant, W. T. Surg. Gyn. Obst., 1938, 67: 722–730.
35. Newell, R. L. Brit. M. J., 1933, 1: 782–783.
36. Ochsner, Alton, Gage, Mims, and DeBakey, Michael. Am. J. Surg., 1935, 28: 669–693.
37. Patterson, R. H. Ann. Surg., 1940, 111: 531–543.
38. Quinn, T. G., and Davison, George. Brit. M. J., 1934, 2: 808–809.
39. Ross, J. P. St. Barth. Hosp. Rep., 1933, 66: 36–39.
40. Serck-Hanssen, Trygve. Acta chir. scand., 1935, 76: 551–560.
41. Southam, A. H., and Bythell, W. J. S. Brit. M. J., 1924, 2: 844–845.
42. Spurling, R. G., and Bradford, F. K. Ann. Surg., 1938, 107: 708–715.
43. Telford, E. D. Brit. M. J., 1942, 2: 96.
44. Telford, E. D., and Stopford, J. S. B. Brit. J. Surg., 1931, 18: 557–564.
45. Theis, F. V. Surgery, 1939, 6: 112–125.
46. Thorburn, William. Med.-Chi. Tr., 1805–1905, 88: 109–123.
47. Todd, T. W. J. Anat. Physiol., 1911, 45: 293–304.
48. Ibid., 1912, 46: 244–288.
49. Ibid., 1913, 47: 250–253.
50. Wanke, R. Arch. klin. Chir., 1937, 189: 513–528.
51. Weber, F. P. Proc. R. Soc. M., Lond., 1912, 6 (pt. 1): 55–57.
52. White, J. C., Poppel, M. H., and Adams, Ralph. Surg. Gyn. Obst., 1945, 81: 643–659.
53. Wilson, S. A. K. Proc. R. Soc. M., Lond., 1913, 6 (pt. 1): 133–141.

RESECTION OF THE KNEE JOINT FOR SUPPURATIVE ARTHRITIS

JAMES E. THOMPSON, M.D., F.A.C.S., CHARLES F. STEWART, M.D., and WILLIAM H. CASSEBAUM, M.D., F.A.C.S., New York, New York

SUPPURATIVE arthritis of the knee joint is a serious disease. Rarely is the joint restored to normal. If the condition persists any length of time, destruction of cartilage and bone is such that a painful knee results. In many cases amputation is required to combat the sepsis which not infrequently results in death. It is not a common condition in civil practice but is a hazard present in all penetrating injuries of the knee.

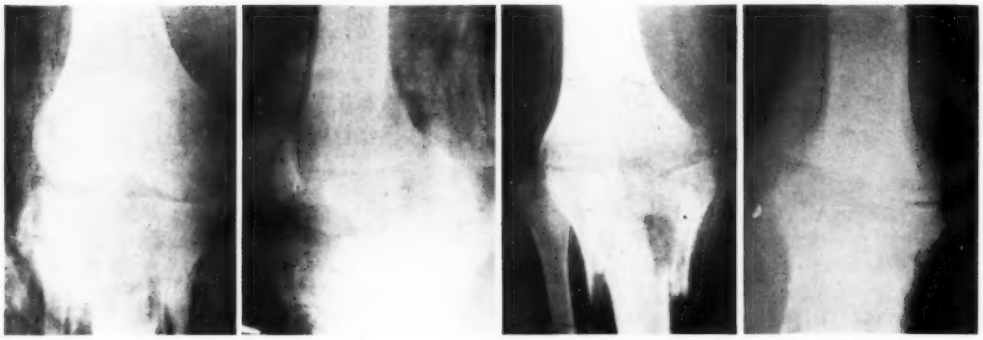
During the early period in which the 9th Evacuation Hospital acted as a general hospital for the French, we encountered 6 patients with wounds of the knee which were either suppurating at the time of arrival or developed suppuration soon after. Characteristic destructive changes occurred in the cartilage of the joint. In 2 of the earliest cases the knees were drained widely by 4 incisions. These incisions were made early in the course of the infection, but the destructive changes occurred despite their use. This result corresponded with our civilian experience; that is that, in a case of suppuration of the knee, no matter what the treatment, the result is a permanently damaged joint.

At about this time we heard of the practice of resection of knee joints in the presence of infection, a procedure the French surgeons had been using for years and one they attributed to Ollier. Naturally, our first reaction to the idea of resection carried out during the course of sepsis was one of violent opposition. It seemed like a very radical procedure to cut through infected soft tissues, bone, and cartilage; to disturb the area of resistance seemed to violate a surgical principle. On the other hand, the French advocates of this procedure pointed out its advantages. Major Curtillet, the consulting surgeon to the French forces, influenced us to try it. As he presented it, the procedure was not new but had been tried prior to the first World War by the French.

In brief, the resection consists of removing the femoral condyles at the highest level attained by cartilage, and the upper half inch of the tibia. The synovia is then excised. The object of the operation is to shorten the course of sepsis by removing feebly resistant cartilage and the areas of infected bone and synovia. Once these become involved, they remain so for a long time. Life and limb are saved by diminishing this period of sepsis, during which the patient becomes very toxic and depleted. The procedure accepts the fact that suppurative arthritis in the knee results in a permanently damaged joint which is either ankylosed or possesses some degree of painful motion. Consequently, the fusion is performed at the earliest possible moment; thus saving the patient time and suffering. The operation removes the suppurating tissues of low vitality which harbor infection, and at the same time secures really adequate drainage. Success is not always achieved. Major Curtillet was frank to say that occasionally nothing is gained and that amputation is not avoided. He did not fear untoward effects from resecting suppurating joints. The optimum time to resect is early, in the first 2 weeks.

Resection of a joint in the presence of infection is often referred to by the French as secondary resection. The term "primary resection" is used for resection done at the time of débridement, and is done because the operator feels that destruction of articular surfaces precludes the return of good function to the joint, and that joint infection will develop. French surgeons do primary resections of practically all joints, even phalanges, though we have seen it used mostly for knees and elbows. We have since resected a few joints ourselves, when the indications were very definite;

From the Surgical Service, Roosevelt Hospital, New York.



a b c d

Fig. 1. Case 2. a, March 4—1 month after wounding, showing extensive tibial fracture and destruction of cartilage of femoral condyle. Detail is obscured by plaster. b, Three months after resection. A little callus is present anteriorly. Only the slightest amount of motion could be produced by manipulation.

namely, when fractures were so extensive that there was no hope of regaining any joint function.

OPERATIVE TECHNIQUE FOR RESECTION OF THE KNEE JOINT

A variety of incisions are used. The transverse incision employed by Major Curtillet seems best. This is an elliptical transverse incision removing the patella. The anterior and posterior cruciate ligaments are divided and the knee joint is flexed—an assistant supporting it with a rolled bath towel in the bend. The femoral condyle is sawed off at a level just proximal to the intercondylar fossa, and the remaining cartilage stripped free from the underlying bone. The tibial condyles are then sawed off as conservatively as possible, but removing all joint surface. Cuts are made so that 5 to 10 degrees of knee joint flexion result. The synovia is completely excised. If a tourniquet has been used it is now removed. Drains are placed at the angles of the incision. One heavy wire suture may be placed through the anterior margins of the bones to prevent forward or backward slipping. A few

a b c d

Fig. 2. Case 3. a and b, Roentgenograms taken February 7, 1944. Circular defect made in posterior part of medial condyle at first operation can be seen on lateral view. There is no detectable erosion of weight bearing surfaces. c and d, Show marked erosion of condyles as seen on March 12, 1944, the day before operation.

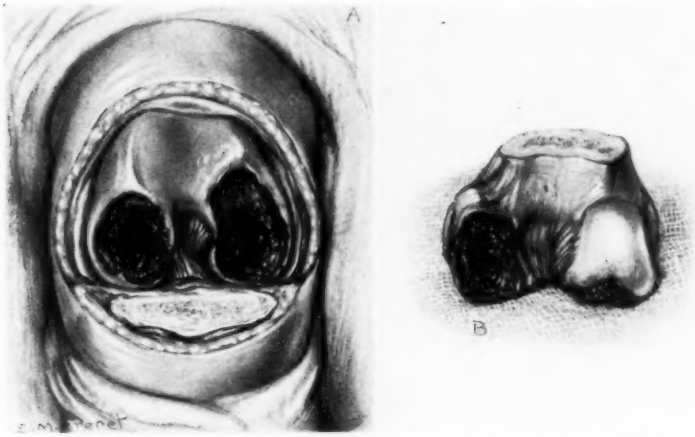


Fig. 3. Drawing illustrating extensive erosion of both condyles of femur as seen at operation.

sutures may be inserted to approximate skin loosely and to prevent retraction. Dressings and a spica are applied. Drains are removed in 5 to 10 days, and the spica is changed as needed. It does not take long for muscle shortening to close the gap. In cases in which the wound is on the posterior aspect of the knee, the wound may be enlarged and used for dependent drainage. Otherwise, one turns the patient, in the spica, face down at intervals. As frequently there remain fractures of the bone adjacent to the resected joint, abscesses, which require drainage, may develop.

It is not our purpose in this paper to discuss the clinical features and course of this disease, but one pathological feature is worthy of note. The earliest destruction of cartilage occurs at the points of contact between the two bones. The greatest damage is found at these points, as the lesions advance. The medial femoral condyle is usually first involved. This observation has been previously described by Phemister and others.

Another point, which experience and previous observations have tended to confirm, is the inadequacy of any prescribed means of draining the knee. We have used 2 large parapatellar incisions, together with a third one behind the medial ligament; and a fourth just posterior to the lateral ligament. Two of the cases about to be described had drainage of this sort. These incisions may relieve the tension of the pus, but pools remain in the deep recesses of the joint, and a film is retained between surfaces in close contact. Here between the condyles and between the menisci and condyles, the film of pus is held by capillary attraction.

CASE REPORTS

Following are 6 case reports which form the basis for this paper:

Fig. 4. Case 3. Roentgenograms taken 6 weeks after operation. Note the evidence of callus formation.

a b

Fig. 5. Case 4. a, March 10, 1944—1 month after wounding. Marked destruction of medial femoral condyle by infection. Early changes are seen in the lateral condyle. b, June 6, 1944—3 months, minus 1 week, after resection. "Fracture line" still visible, but with callus seen at margins. Knee solid clinically.

Case 1. This patient, a Tunisian Arab, was wounded by a bullet on January 27, 1944, at 8:00 a.m. The missile entered the left knee medially and made its exit through the posterior aspect of the upper third of the calf. After 24 hours, first aid treatment was given, including local sulfanilamide powder. About 64 hours after injury, the patient was operated upon in a mobile French hospital. At operation, it was found that the knee joint had been opened, and that there was an incomplete fracture of the medial tibial condyle. The knee joint was not closed; the wound was débrided and the leg placed in a cast.

Ten days after injury, the patient arrived. He appeared acutely ill, and pale, but his temperature was normal. He complained bitterly of pain in his knee, and, because of this, on the following day, the cast was removed, and the wounds were dressed. Because of diffuse swelling in the knee region, and extreme pain on motion, suppurative arthritis was suspected. The wounds were dressed and a cast was reapplied. The patient's temperature rose thereafter and ranged between 101.8 and 104.8 degrees. On his 4th day in our hospital, the knee joint was aspirated and cultured (Bacillus hemolytic streptococcus). Incisions were made into the knee joint at four places, and three Penrose drains were placed in the joint. Despite repeated transfusions and parenteral sulfonamide therapy, the patient continued to run a septic temperature curve. This septic course continued; the patient lost his appetite, suffered occasional chills, and looked extremely ill. Finally, 23 days after admission and 20 days after drainage of the knee joint, amputation was decided upon as the only procedure which would save the patient's life. Resection of the joint was considered, but abandoned as we had had no experience with it. A guillotine amputation through the lower third of the left thigh was done. The amputated knee revealed extensive periarticular edema. Covering the entire edematous synovial lining of the joint was a hemorrhagic fibrinous exudate. There was destruction of the cartilage on the weight-bearing surfaces of the femur and tibia down to the bone. Progress following amputation was satisfactory.

Case 2. This young adult Arab was wounded on February 3, 1944, by a bullet which perforated the upper tibia from behind forward. The fracture was badly comminuted and was of the inverted "V" type with the fracture lines extending into the joint. Excision of the wound of exit and wound toilet were performed at a French evacuation hospital about 24 hours after injury.

On his arrival on February 12, 1944, the patient seemed quite ill and had a fever of 103 degrees. Next day the cast was removed, revealing a wound 3 by 2 centimeters about 5 centimeters below the patella, and another wound 1 centimeter in diameter in the popliteal space. The anterior wound, which was discharging foul, blood-tinged pus was enlarged. Sulfanilamide powder was instilled and a plaster applied. X-ray film revealed the fracture described and several small foreign bodies about the fracture site. A blood count on February 18 revealed a hemoglobin of 54 per cent, Sahli; red blood cells, 2,900,000; white blood cells, 34,200; with 75 per cent polymorphonuclears. After the drainage procedure the fever dropped to 99 degrees and remained so for only a few days.

During the succeeding 3 weeks the patient ran a septic course, and went progressively downhill. He had surprisingly little pain. In this period he received intensive plasma, blood, and sulfadiazine therapy. On March 4 x-ray films showed osteomyelitis of the tibial condyle, narrowing of the joint space, and evidence of destruction of condylar cartilage,—the picture of acute suppurative arthritis. Serum protein was 5.6 milligrams per cent; hemoglobin, 69 per cent; red blood cells, 3,980,000; white blood cells, 20,000; polymorphonuclears, 80 per cent.

On March 11—5 weeks after injury—there was foul-smelling pus exuding from both anterior and posterior wounds. The knee joint was distended.

a b a b

Fig. 6. Fig. 7.

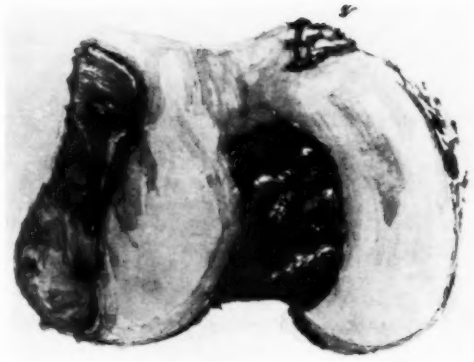


Fig. 6c.

Fig. 6. Case 5. a and b, Preoperative roentgenograms. Patella is absent. Eroded area could be seen on films. c, Illustrates ulcerated area of medial condyle found at operation.

Fig. 7. Case 5. Roentgenograms taken 6 weeks after operation. There is early evidence of callus formation.

Resection of the knee joint was decided upon and done that day. A "U" incision, base upward, was used. The joint was filled with thick, gray pus. The femur was sawed across at the highest point reached by the articular cartilage. The tibial articular surface was resected with rongeurs and curette. It was impossible to do otherwise as the large condylar fragments were so free; and we were anxious not to disturb the remaining bone and its blood supply. The edematous synovia was excised. Dressings and a spica were applied after placing drains laterally and medially. The leg was held so that an inch gap between the bones was maintained. No suturing of the skin or flap was done, but the patella was removed. Cultures made at the time of operation grew β hemolytic staphylococcus, and a β hemolytic streptococcus. One thousand cubic centimeters of blood was given postoperatively.

Examination of the excised specimen showed a large area of destruction of the medial femoral condyle. The same type of lesion involved the lateral condyle, but to a lesser extent. On both sides bone was involved, but only a few millimeters were necrotic. The cartilage of the contact surfaces of the tibia was also gone, but destruction of the underlying cortex was minimal. The menisci though still present, were soft; and the sharp inner edges dissolved. The periarticular tissues were slightly swollen.

Liberation of pus is thought to account for the abrupt fall in temperature which resulted. The patient's immediate postoperative course was very satisfactory with the temperature remaining near normal. Two and a half weeks after resection the patient developed a spiking fever and a large abscess communicating with the fracture and extending down the lateral anterior fascial compartment of the leg was drained. Culture of this abscess showed that Bacillus pyocyaneus had been added to the organisms originally present.

Improvement following this drainage was short-lived and 10 days later, on April 8, a pooling of puru-

a b

Fig. 8.

a b

Fig. 9.

Fig. 8. Case 6. a, Preoperative roentgenograms taken March 8, 1944. b, Preoperative roentgenogram taken March 14, 1944. Note the extensive loss of substance of upper part of shaft of tibia, with the marked comminution of fragments.

Fig. 9. Case 6. Roentgenograms taken on May 4, 1944, 43 days after operation. Small sequestra can be seen adjoining defect of tibial shaft. The lateral view gives evidence that the defect is being bridged by new bone.

lent drainage noted between the ends of the femur and tibia, was drained posteriorly. During this procedure, an old hematoma, anterior to the tendon of the semimembranosis muscle was found and evacuated. At the same time moderately deep jaundice was noted as well as splenic enlargement. The jaundice was felt to be due to a nonhemolytic transfusion reaction. During this period (March 29 to April 15) penicillin became available and was given. The temperature remained normal after the second drainage and remained so until the patient was evacuated May 31. At that time he could raise the limb off the bed without pain. When the knee site was tested for motion a minimal amount could be produced and this was painful. All wounds were healed except a small granulating area 1 by 1.5 by 2 centimeters deep between the tibial condyles. The knee site was kept immobilized to promote union. His general condition was excellent. Roentgenograms on May 31 showed the bones in perfect apposition and the leg straight. There was a little callus visible at the anterior edge of the tibia. Between the condyles of the tibia was an area of decreased calcification. No evidence of sequestra was present.

This was the first case in which resection was performed. Resection should have been done much earlier. The complicating abscesses were due to osteomyelitis of the fractured tibia. It was this, in fact, which had led to suppuration of the knee, as the missile had not passed through the knee joint. The immediate response to resection was excellent. Adequate drainage was obtained. Although the course of the infection was long, it would have been longer—and the toxemia greater—had the knee not been resected. Life and limb were being threatened. Bony union had not been obtained at the time of evacuation (4 months after injury, and about 3 months after resection). It is believed a satisfactory union, bony or fibrous, will result. Residual infection in the tibial condyles and our failure to place the bones in apposition soon enough, and general debility are the possible causes for the failure to secure early fusion. The extensive, comminuted fracture was a bad set-up for any treatment.

Case 3. This white French soldier received a shell fragment wound in the outer aspect of the right knee on February 2, 1944, at 10:00 a.m. At 8:00 a.m. on February 3, 1944, he was operated upon at a French evacuation hospital. The shell fragment was removed from the posterior part of the lateral femoral condyle through a posterior incision in the popliteal space. This approach traversed the joint. The entrance wound was incised but not débrided.

Four days after wounding he was admitted to hospital complaining of pain in the knee and with a fever of 100 degrees. He gave a history of chronic malaria, recently treated.

Inspection of the wound showed a long, clean, granulating, vertical incision. The wound of entrance was now 1½ inches long and situated just above and anterior to the head of the fibula. Pressure on the suprapatellar pouch caused clear synovial fluid

to exude. During the subsequent few days this fluid became purulent as his temperature rose to 102 degrees.

On February 11 the knee joint was drained under pentothal anesthesia. Two anterior incisions were made as well as posterior ones. These latter drained the posterior portions of the joint behind the condyles. Penrose tubing was inserted. It was interesting to note that relatively clear joint fluid was obtained through the posterior incisions while frank pus was present in the suprapatellar pouch. A smear of this showed staphylococcus.

During the following month the patient's course continued septic. Temperature peaks varied between 101 and 102 degrees. The resulting anemia (red blood cells 2,890,000; and hemoglobin, 61 per cent) was combatted successfully with six blood transfusions (blood count on March 12, red blood cells 4,600,000; hemoglobin, 78 per cent; white blood cells 11,500). Sulfadiazine irrigations and immobilization in a spica did not prevent destructive changes in the joint as shown by x-ray on February 26. Roentgenogram revealed narrowing and early necrosis of the bone of the medial and lateral condyles. After consultation with Major Curtillet of the French Army a resection was done on March 13.

Under general anesthesia and with a tourniquet in place, the lower ends of the two lateral drainage incisions were extended distally and curved to meet, thus forming a U. This incision included all layers. The patella was excised. After the cruciate ligaments were severed, the knee joint was flexed and the femur dislocated anteriorly into the wound. About 1¾ inches of the femoral condyles were removed with a saw, all the joint surface being removed. Approximately a half inch of the tibial condyles was then sawed off. Following this all the remaining synovia was excised. The U flap was sutured with two wire sutures, wide open drainage sites being left laterally. No drains were inserted. The raw bony surfaces of the femur and tibia were placed in contact in 5 degree flexion, and a spica was applied.

A culture of the pus obtained at operation showed β pyocyaneus and a diphtheroid bacillus. The joint had contained pockets of white, thick pus, and all the contact surfaces of the femoral and tibial condyles were eroded. The menisci were completely dissolved and the cruciate ligaments had almost disappeared. The synovia was edematous and hemorrhagic.

During the first month after operation his temperature course continued to suggest sepsis. His spica was twice changed and the local areas found to be doing well. Finally on April 9 after a temperature rise to 104.2 degrees, accompanied by tenderness over the liver, a positive smear for malaria (Plasmodium vivax) was obtained. Malaria had long been suspected but previous smears were negative and no therapy was given until this time.

Under atabrine therapy his temperature returned to normal. On April 18 an x-ray film showed callus developing (5 weeks after operation). Clinically the knee fusion was firm under gentle manipulation. Two weeks later the spica was discarded, and a cast was applied. The patient was soon up and around walking with crutches. On June 1 he was evacuated to Africa.

A letter from him in August of the same year stated his wounds were well healed and that he was bearing weight though still using crutches.

This case represented a very severe staphylococcus suppurative arthritis of the knee, complicated by recrudescence of an old chronic malaria. His marked sepsis produced a profound secondary anemia that required many transfusions. In the light of more recent experience, arthrotomy with thorough cleansing of the joint, irrigations and local penicillin instillations (which was not then available) might have cleared up the impending suppuration, if it had been performed during the first few days after admission. His progressively downhill course makes us believe that it would have been necessary to amputate his leg in order to save life, if the arthrectomy had not been performed. His primary treatment can be criticized for its failure to close the deep layers of the wound of entrance, and in applying a midthigh cast instead of a spica.

CASE 4. This 32 year old Tunisian Arab was wounded at 11:00 a.m., February 2, 1944, by shell fragments. Forty-eight hours later, he was operated upon at a French evacuation hospital, and the following is a summary of their note:

Left leg. Compound fracture of the lower tibia. The wound was excised, and 2 other large wounds of the same leg were débrided radically. A comminuted fracture of the medial femoral condyle with an opening into the knee joint was treated by excision of the entrance wound and establishment of through and through drainage of the suprapatellar pouch, half inch rubber tubing was used. The leg was immobilized in plaster to the hip. In addition large wounds of the right calf and left hand were present.

The patient was received by us on February 6, 1944. His temperature was 101 degrees, pulse rapid, and he was stoically bearing considerable pain. The wounds were inspected the next day and this note was made: "Has an open wound of the left knee, with projecting, heavy rubber tubes. These removed. Some gray-yellow slough, where there has been contact between the wound edges and the rubber tube drains. It would be impossible to close the joint. There is no swelling of the knee. [Other wounds then described.] All wounds clean. Sulfanilamide, vaseline gauze and a cast applied to left knee." Culture of the tracts into the knee joint later grew Staphylococcus albus and a diphtheroid bacillus.

The patient was given supportive treatment consisting of plasma, transfusions, sulfadiazine, vitamins and iron.

During the next 12 days the patient's pain diminished somewhat, but fever, with daily rises to 102 or 103 degrees persisted. On February 13 his hemoglobin was 54 per cent; red blood cells, 2,520,000; white blood cells, 10,250, with 76 per cent polymorphonuclears. February 19 the patient was re-dressed. There was little tenderness, and no destruction of the joint, but pressure on it caused a slight synovial leak. It was felt that the fever was due to his other wounds, especially the compound fracture, which presented a small pool of brownish pus.

On March 10 the cast was again removed, and at this time any movement of the knee was painful. There was some periarticular swelling but no increase in joint fluid. An x-ray film showed "evidence of marked bone destruction involving practically all the articular surfaces of the knee (Fig. 5). Destruction is particularly marked in the region of the medial femoral condyle." Fever to 102 degrees daily persisted.

On March 15 the knee joint was resected. During preparation of the leg, flexion caused the now closed medial drainage wound to pop open and discharge some granulation tissue. No other fluid was present in the joint. Destruction of cartilage and bone was noted on the contact surface of the medial femoral condyle. The medial tibial condyle showed less marked destruction. Some of the medial meniscus had been digested. The synovia was gelatinous. The lateral condyles of femur and tibia were eroded of cartilage, where there had been contact. Cultures made from the joint fluid grew a weakly hemolytic Staphylococcus aureus. The operation was performed by Major Curtillet, French consultant surgeon, who resected an inch of femoral condyle and the articular surface of the tibia. A single wire suture was placed in the bone ends to prevent the surfaces losing contact and sliding back and forth. Rubber tube drains were placed at the lateral and medial ends of the transverse incision through which the patella had been removed. The wound edges made contact without suture. The knee was flexed 15 degrees. A spica was applied.

Before operation the patient had received 6 transfusions of 500 to 600 cubic centimeters each. The last two were accompanied by rather severe reactions. The preoperative blood count was: hemoglobin, 64 per cent; red blood cells, 3,200,000; white blood cells 5,900, with 63 per cent polymorphonuclears.

The temperature course during the next 17 days was not changed by the resection. During this period the spica was twice changed. The drains were removed on March 25—10 days postoperative. Cultures at this time showed that the Bacillus pyocyaneus as well as the staphylococcus was now present in the wound.

When we obtained some penicillin the patient was given 1,270,000 units during a 6 day period (March 28 to April 3). In the subsequent 2 to 3 weeks his temperature gradually fell to normal. His blood count on April 15 was: hemoglobin 71 per cent; red blood cells, 3,580,000; white blood cells, 7,400, with 52 per cent polymorphonuclears.

The patient's wounds were skin grafted on May 4, and he was finally evacuated to Africa June 18—4 months after being wounded. The knee was solid and weight had been borne in spite of a nonunion of the fracture of the lower third of the tibia. The "fracture" line between the condyles was easily visible by x-ray, and there was little callus. However, one would not have hesitated to allow weight bearing had it not been for the leg fracture.

A letter written by him on August 2, 1944, from Africa stated that union of his leg fracture had not yet occurred.

As far as the knee is concerned, this patient's convalescence was shortened by resection. With the amount of joint destruction which occurred, any motion would have been painful, and there would have been deformity as well.

In retrospect, we believe thorough débridement—even 48 hours after wounding—with closure of the joint, might have prevented infection. Under the newer program to be described later, we too could have closed the joint and prevented suppuration. In our opinion a joint left open for whatever reason should never be dressed until it becomes sealed by granulations, otherwise infection will develop. Contamination occurs during dressings no matter how carefully they are done.

Case 5. This Arab received a perforating shell fragment wound of the right knee on March 3, 1944. The patella was comminuted. The shattered patella was removed and the popliteal space débrided at a French evacuation hospital.

He arrived at our hospital on March 7, 1944, in good condition in a hip spica. An x-ray examination revealed the absence of the patella and slight erosion of the anterior surface of the external femoral condyle. On March 11, because of pain and a slight fever, his knee was inspected. At the lower end of a U shaped Ollier incision a small portion of the femoral condyle could be seen. The wound edges appeared healthy and with a little undercutting the joint was closed without tension, fine wire sutures being used. The vertical popliteal wound was partially closed.

The joint infection became more apparent. Patient's temperature rose to 102 degrees. He developed an anemia and his blood count was, red blood cells, 3,020,000; hemoglobin, 61 per cent; white blood cells, 10,400, with 77 per cent polymorphonuclears. Culture of the pus from both anterior and posterior incisions revealed Staphylococcus hemo-

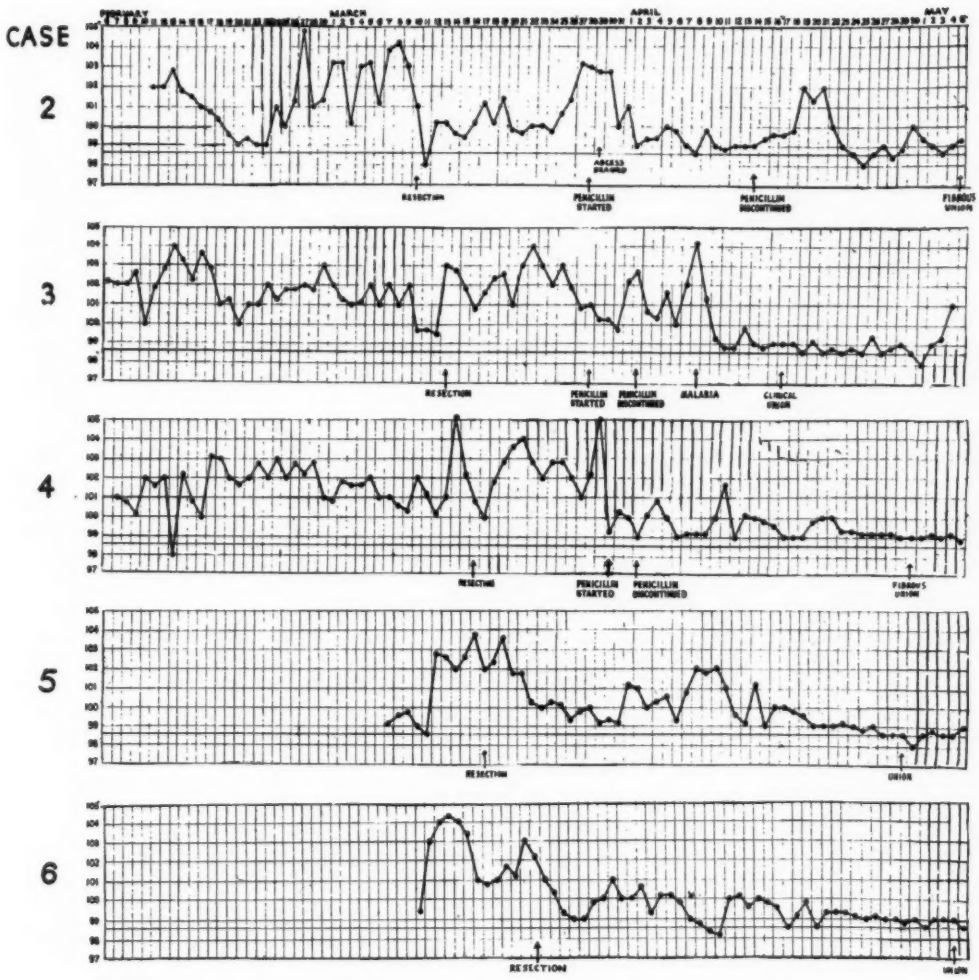


Fig. 10. Chart showing highest daily temperatures in Cases 2 to 6.

lyticus and Bacillus pyocyaneus. A roentgenogram showed joint narrowing and further erosion of the external femoral condyle.

On March 17 an arthrectomy was done, with removal of 1 inch of the femoral condyles and ½ inch of the tibial condyles. The synovia was completely excised. A small area of the medial femoral condyle had been eroded down into the cancellous bone. The joint contained considerable pus. Following removal of the condyles, two wire sutures were placed through the anterior edges of the cortex of both bones to hold them in proper approximation. Drains were placed at the lateral angles. A hip spica was applied.

The patient's postoperative progress was very satisfactory and by May 4 (7 weeks) callus between the fragments was seen by x-ray. His temperature had not risen above 99 degrees. One complication, a foot drop, developed postoperatively and was still present at the time of his evacuation to North Africa on June 1.

Arthrectomy was performed very early after the first evidence that suppuration and

joint destruction existed. In the light of later experience an attempt at cleaning the joint with irrigations and instillations of penicillin after closure of the synovia should have been done. The joint should not have been left open at the time of original débridement. The cause of the complication, foot drop, was not apparent though it is a well known result of cast pressure on the head of the fibula.

CASE 6. This French Arab soldier was wounded by a shell fragment near Cassino, Italy, on March 1, 1944. He suffered a compound comminuted fracture of the right tibia extending into the knee joint. Débridement was performed and a midthigh cast was applied at a French evacuation hospital.

On admission to our hospital 7 days later on March 8 a roentgenogram revealed considerable loss of bone substance. Examination showed a large, gaping wound anteriorly, about 3 to 4 inches below the knee joint. Loose fragments bathed in pus lay in the wound. A blood count showed red blood cells, 2,410,000; hemoglobin, 54 per cent; white blood cells, 6,850, with 57 per cent polymorphonuclears.

During the following 5 days the patient developed a suppurative knee joint in spite of immobilization in a spica, and transfusions totalling 2800 cubic centimeters of whole blood were given. He received sulfadiazine 1 gram every 4 hours. Aspiration of the knee joint on March 17 showed cloudy fluid containing Staphylococcus aureus. The concentration of sulfadiazine in the joint fluid was 6 milligrams per cent. In the blood the level was 8 milligrams per cent. Blood proteins were normal 6.7; albumin, 4.9; globulin, 1.87. By March 21 his temperature reached 103 degrees after a chill. It was felt that arthrectomy might preserve a limb which otherwise would have to be amputated.

On March 22 arthrectomy was done, the technique being that described in the previous cases. The transverse elliptical incision, excising the patella, was used. One inch of femoral condyle was removed. The cartilage was removed from the tibia with chisel, curette and gouge. The joint contained thick pus in which a pleomorphic gram-positive bacillus was found. The medial femoral condyle was eroded. The cartilage of the tibial condyles was soft and already separated in part. The fracture line extended across both tibial condyles transversely (Fig. 9b). A hole in the superior surface of the external tibial condyle communicated with the fracture below. This area in the depressed lateral condyle, was enlarged to increase the drainage. The other joint structures were normal. The wound was loosely closed with a drain at either angle. A spica was applied.

After operation the patient required several blood transfusions to restore his blood volume, but his temperature never rose above 100 degrees. Six weeks after operation, on May 4, union at the joint was firm clinically and the x-ray revealed callus formation between the femur and tibia. Several sequestra were present at the fracture site and these were removed during subsequent weeks. The wound was considerably smaller when the patient was evacuated to North Africa on June 1. He was then walking with crutches, wearing a cast on his injured leg.

This case represents indirect penetration of the knee joint by means of a compound fracture involving the tibia. Without doubt arthrectomy saved the limb in this case.

ANALYTICAL SUMMARY OF CASES

Five patients with suppurative arthritis have been subjected to arthrectomy during an active stage of the joint infection. In none was there any local flare-up, or signs of increased sepsis; rather, there was either no immediate change (Cases 3, 4), or an improvement resulted (Cases 2, 5, 6). Nothing occurred which would lead one to believe that the interference had broken down any defensive wall the body had built up. It should be noted, however, that the suppurative arthritis in these cases followed damage to the joint. It is possible that suppurative arthritis, of hematogenous origin, in which presumably the bacteria have invaded healthy tissues, may not respond in the same way.

While other factors, such as multiple wounds (Case 4), malaria (Case 3), and extensive fractures of the tibia (Cases 2, 6) have clouded the picture, these patients have benefited from resection, and the course of joint suppuration has been shortened. One patient (Case 2) may not develop bony fusion; but if the fibrous union is not satisfactory, the fusion can be attempted again later. In this case the bony surfaces were not apposed until covered by granulations.

In our opinion, the technique of the resection may be modified to obtain an extremity of more optimum length. We believe it important to remove less of the femoral condyle in order to preserve length, provided one removes all the necrotic bone and diseased cartilage. We have not seen destruction of bone so extensive that it could not be removed by resection of ½ inch of the femur. The remaining cartilage and any subchondral necrotic bone could then be ronguered or chiseled away. The tibial resection can be done very conservatively with a rongeur and curette.

If less bone is removed it is obvious no skin should be excised.

Resection of joints during suppuration has, we believe, a place in American surgery. It is to be hoped that better surgery and penicillin will make its place a small one. Prevention, according to a plan first advocated by Colonels Hampton and Lyons, made such strides that the number of suppurating joints markedly decreased. We subsequently performed arthrotomies on 202 penetrating wounds of the knee joint, and although our follow-up is limited we are reasonably sure that few have developed suppuration. The necessity of sometimes evacuating large numbers of patients did not permit us to be certain of a few of them who were evacuated within several weeks of injury. Many of the group were undoubtedly saved from developing knee joint infection by application of the plan here outlined.

The plan emphasized arthrotomies through adequate incisions of the joint whenever the presence of infection or devitalized tissue in the joint is suspected. A thorough débridement is then done, with removal of foreign bodies, blood clot, and devitalized bone and cartilage. The joint is irrigated and the synovia is closed. Before closure 10,000 units of penicillin is placed in the joint. Irrigation with saline through a large needle and injection of penicillin are repeated if indicated. A spica must be used for adequate immobilization. Blood volume is restored by multiple transfusions.

The "penicillin program" as outlined will undoubtedly reduce to a minimum knee joint suppuration and we believe it should be carried out before resection. We also believe that drainage may be attempted before decision is made to resect. If, despite drainage, the suppuration persists and destructive changes become visible by x-ray, resection should be recommended. This program may bring resection into the picture later than the optimum time for it and later than the French recommend. However, the present results obtained by the combination of good surgery, closure of the synovia, penicillin, and blood restoration seem to justify the delay.

SUMMARY AND CONCLUSIONS

1. Six cases of knee joint suppuration, following shell fragment wounds, are reported.

2. In 1 case amputation was done and the joints were resected in the remaining 5.

3. The resections were done during an active stage of suppuration.

4. No patient had any immediate reaction to the resection which was unfavorable. In 2 who needed drainage (Cases 2, 6), the reactions were immediately favorable.

5. It is believed that the course of the infection has been shortened and that the resulting fusion of the knee is an acceptable end-result.

6. It is believed this procedure properly carried out will frequently save life and limb by shortening a suppurative infection which not infrequently threatens both.

7. It is believed that a program of wide arthrotomy and thorough débridement with closure of the joint when possible, together with penicillin therapy, transfusions as indicated, and adequate immobilization, will prevent knee joint suppuration in war wounds.

BREAST CANCER

HERBERT C. CHASE, M.D., F.A.C.S., New York, New York

BREAST cancer is the most common type of neoplasm, having almost twice the incidence of that of the next site, the cervix (Fig. 1). Thirty-seven of every 1,000 women who reach maturity will become victims of this disease and more than 15,000 women die annually from it in the United States (Fig. 2). Moreover, carcinoma of the breast is increasing at the rate of nearly 1 per cent per annum and is not a preventable disease. Cancer of the lip, the tongue, the skin, and the cervix are lesions which, in a measure, may be prevented, but so little is known of the etiology of breast cancer that little hope can be entertained at present as to its prophylaxis.

Yet, the present outlook in breast carcinoma is by no means discouraging. The facts and figures are all to the contrary and show that the prognosis is increasingly hopeful and constantly improving (Table I and Fig. 3). Of the 15,000 women who die annually, 10,000 can be saved by surgery alone if the lesion is discovered while confined to the breast (Fig. 4). (This means a salvage of 29 of the 37.) After the disease has spread to the axilla only 6,000 can be saved by surgery, x-ray, and radium combined (Fig. 5). Our greatest hope for continued progress in the problem of breast cancer lies in a program of education of both patient and practitioner toward early diagnosis; and in the education of surgeons toward a more thorough, extensive, and meticulous radical operation.

Women are coming earlier and more regularly for examination of their breasts, and it is becoming increasingly infrequent to find advanced lesions. They readily accept the necessity for surgical exploration of breast tumors, more readily it would seem at times, than some physicians. This program of education of women should be continued and encouraged and everyone in the profession—every doctor and nurse—should become a well informed participant in it. Women past 35 years of age should be advised and taught to examine their breasts monthly during the mid period. This will place a good part of the responsibility where it will best be met—on the patient herself. She will educate others. This instruction is not so likely to produce unfounded fears as it is to lead to the satisfaction which comes from early discovery of any lesion which may arise.

A slow but steady improvement is being made in the radical breast operation. Surgeons, realizing that standardization is often a barrier to progress, are getting away from the old limited orthodox types of procedure such as the Halsted and Willy Meyer. With a broader concept based on the more recent elucidation of the pathology, the modes of spread, the routes and pathways of spread, and with an intimate knowledge of the anatomy, the radical dissection is being extended and we are operating not only with our eye but with our mind's eye.

Sampson Handley has made two definite additions to the radical breast operation: a wider area of fascial removal and removal of the epigastric nodes. For many years we have constantly emphasized:[1] (a) the necessity of a systematized procedure to gain thoroughness; (b) the necessity of completely mobilizing skin flaps for better exposure and haemostasis; (c) the removal of all superficial fascia from the skin flaps; (d) a method to avoid handling or squeezing the breast during the operation; (e) a method to insure the removal of all five groups of nodes (including subscapular and epigastric); (f) an antiseptic technique, to avoid implanting the field with cancer cells during the operation. This is a reality. We have repeatedly demonstrated in our clinics cancer cells in stained smears made from gloves, instruments and in the centrifuged sediment from the saline of the hand basins in the operating room—also there are a few case reports of implantation of cancer into the donor site when skin grafting was done at the time of the radical operation.

[1]The radical breast operation. Surg. Gyn. Obst., 1938, 67: 97.

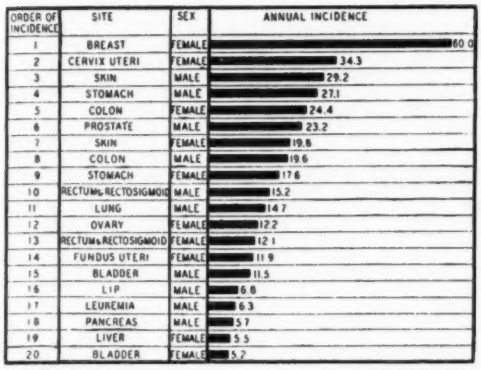


Fig. 1. [Chart showing average annual incidence rates of breast cancer per 100,000 population, New York State, exclusive of New York City, 1942, 1943, 1944.

A more thorough technique, a greater dissemination of proper technique, and its more regular use by larger and larger groups are some of the basic reasons for gradual improvement in results. There has also been gradual improvement in x-ray equipment, higher voltage machines, improved methods (Coutard, etc.) and technique, all of which has meant added success.

Early diagnosis continues to be of paramount importance, this one factor counting for the salvage of 4,000 additional women each year. While it is not possible nor appropriate to go into the details here, of the diagnosis and differential diagnosis of breast cancer, certain vital facts should be repeatedly emphasized. (1) Seventy per cent of all breast lesions admitted to the hospital are malignant. (2) Peau d'orange, elevation or retraction of the nipple, axillary node involvement are the signs of advanced carcinoma of the breast and it is negligent to await their development. (3) A knowledge of three simple lesions, fibrocystic disease, fibroadenoma and cysts will, together with carcinoma, comprise the diagnosis in 87 per cent of cases. (4) The patient with fibrocystic disease is five times more likely to develop cancer than the corresponding age group with normal breasts (Fig. 6). This is the only type of breast lesion in which "observation" and repeated examination is indicated and safe. (5) Most important of all, it should be repeatedly emphasized that there is *not any kind* of discrete mass in the breast that does not require removal and microscopic examination. The policy should always be "look and see," not "wait and see." If there is a discrete mass, observation is neglect. Carcinoma often masquerades as mastitis and mastitis masquerades as carcinoma. This is particularly true in the diffuse papillary type of fibrocystic disease and in the menopausal woman with ectasia and periductal mastitis. (6) It should also be emphasized that the commonest of all breast lesions (fibrocystic disease) is the most difficult to differentiate when localized and the very one in which cancer is most likely to occur. These facts make frozen section imperative in this type. (7) Bloody discharge from the nipple means carcinoma until proved otherwise. About 50 per cent of papillary cystadenomas and intraductal papillomas become malignant. (8) Skin dimpling, fixation, or tethering is one of the latest of the early signs and one of the earliest of the late signs. Do not depend on it nor wait for it. (9) Axillary nodes are not palpable in 30 per cent of cases when involved. Another 30 per cent will show only hyperplasia in breast malignancy. (10) In about 95 out of 100 times, the diagnosis can be made in the "gross" when the lesion is removed. In the five doubtful or borderline cases, frozen section is a reliable procedure. Aspiration biopsy is of definite but limited value. A negative means nothing. It is of limited application because many lesions by their very nature require a tissue pattern for

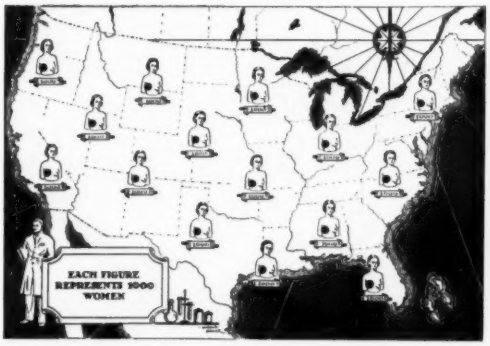


Fig. 2. Fifteen thousand women die annually in the United States of breast cancer.

Fig. 3. The American College of Surgeons, 1945 report. Of a total of 2,636 cases there were 57.3 per cent cures. Two per cent were less than 30 years of age. Best results were obtained in the 35–50 year age group; poorest results in 50–60 year age group. Heredity was a factor in 20 per cent. Nulliparas numbered more than two to one.

TABLE I.—RADICAL OPERATIONS—5 YEAR CURES

Period	Consensus reported per cent
1890–1900	18
1900–1910	25
1910–1920	30
1920–1930	42
1930–1940	50
1945—American College Surgeons	57.3

differentiation. Inasmuch as *each and every* discrete nodule in the breast requires removal, aspiration biopsy is an unnecessary procedure. It may, when negative, confuse the picture and lead to refusal of operation. There is nothing which will replace the satisfaction of getting the gross specimen in one's hand and examining it. I am sure we shall all save more lives that way.

Regarding the etiology of mammary carcinoma, little can be said and less proved. Recently many facts have developed which have led to interesting speculation. The hereditary factor is difficult to evaluate. The impressive experiments of Maud Slye in the inbreeding and outbreeding of cancer mice have been repeated and confirmed by many observers. In the human, organ specificity seems to be the most important consideration in heredity and is present in 20 per cent.

The effect of estrogens continues to be stressed and cancer of the breast has been produced in both susceptible and nonsusceptible strains of mice by administering estrogens in large quantities for prolonged periods. Many clinicians have reported cases of breast carcinoma following prolonged treatment of menopausal women with estrogens in high dosage. While these reports are not conclusive, and while it is a fact that the doses given are far in excess of the physiological titer, they are impressive, and suggest that great caution should be used and estrogens should not be given to any woman in amounts greater than normally occurring; and none at all to women with a family history of carcinoma, especially of the breast; and none to women who have been operated upon for cancer of the breast; nor to any woman with a breast tumor of any kind before or after operation or other treatment.

To the clinician, breast stasis and arrest of function continues to be the most important and impressive predisposing factor in the development of breast cancer. The lesion is more common in the nullipara by nearly 2 to 1. Cessation of lactation produces a more profound and complete involutional effect on the human breast than any other factor. In keep-

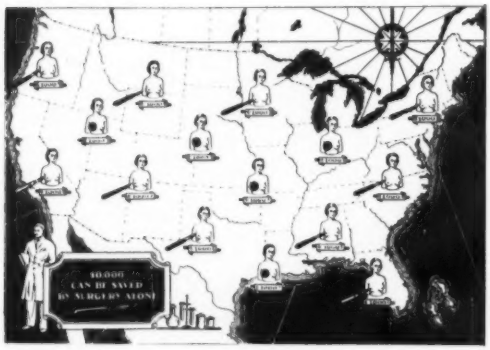


Fig. 4. Ten thousand (of the 15,000) can be saved by surgery alone, while the lesion is confined to the breast.

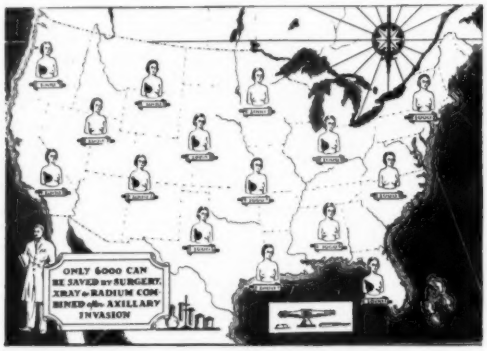


Fig. 5. Only 6,000 can be saved after the axillary nodes are involved.

ing with these facts are the statistics of China. For centuries dating back to the Ming Dynasty (1368-1462 A.D.) Chinese women of the upper or Mandarin class have abhorred large breasts (and large feet). It has long been their custom to bind their breasts as soon as the baby is born and turn the infant over to an Amah (wet nurse). The statistics of China show that the incidence of carcinoma of the breast among the Mandarin women is the highest in the world and among the Amahs, the lowest recorded. Castration produces no such involutional effect on the breast. In fact the anterior pituitary and adrenal cortex make up a compensatory mechanism for the manufacture and excretion of steroids to the end that after castration the estrogen titer is often up to or in excess of normal. No such biologic compensatory mechanism exists in the male and the results of castration for breast cancer in the male are more profound and lasting and compare with or even surpass those seen in prostatic carcinoma. Castration seems to be more effectual in the prevention of breast cancer in susceptible strains of mice and when done before the animal reaches maturity cancer rarely develops. This is similar to the observation I have mentioned many times—that it is extremely rare to see carcinoma of the breast in bitches which were spayed young, i.e. before their first heat.

It is interesting to note also that the thyrotropic hormone of the pituitary has been used to offset the stimulating effect of estrogenic hormones in cancer susceptible strains of mice. In this connection, it should also be recalled that a "duct growth hormone," a separate and distinct entity has been isolated by Taylor and Turner (Bureau of Animal Husbandry, Veterinary Experimental Station, Maryland). Not only does this duct growth hormone increase the development of milk ducts but its effects are so marked in developing the udder in both open and bred heifers that its commercial possibilities in the dairy industry are being investigated.

In the past few years a great deal of interest has been aroused by reports of the "milk factor" in breast cancer by Bittner and his associates. Research workers in Holland and in Bar Harbor, Maine, concluded about the same

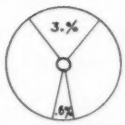


Fig. 6. Comparison of the incidence of carcinoma in normal breasts and in breast affected by fibrocystic disease. The ratio is 5 to 1.

time and independently that transmission of breast carcinoma to the offspring in susceptible mice strains was through the mother and extrachromosomal. With this basic fact in mind, Bittner and his co-workers have shown that in strains of mice susceptible to breast cancer, if the litter is allowed to nurse their mother although she has not cancer of the breast, the females of the litter develop the disease. If the females of the litter are given over to a foster mother of noncancerous strain they do not develop the disease. It was found, also, that if these susceptible female offspring nursed their mother only once the lesion developed and, only by placing them with a foster mother before they nursed their own mother at all, could the disease be prevented; and this prevention was absolute. A more striking fact is that by carrying out the experiment in the opposite direction, cancer of the breast was implanted in strains of mice having no such susceptibility. A single nursing not only establishes the factor in the young female but in all her descendants and whole races of mice can be saved from developing mammary carcinoma by preventing them from nursing their mother at all.

The milk factor does not produce its effect immediately. It reaches the breast through the intestine, apparently increases in quantity as the breasts develop and when the mouse grows old cancer develops in her breast. In the meantime she has transmitted the factor to the females of each successive litter. In some highly susceptible breeds, this happens in every individual. The milk factor is present in large amounts in the breasts of these individuals and although it will not produce the disease directly when injected into other aged individuals, one millionth of a gram of mammary tissue yields enough of it when extracted with saline to confer the disease on an endless series of animals. A great deal of experimenta-

TABLE II.—EFFECT OF EXTENT OF AXILLARY METASTASES ON SURVIVAL*

	Cases	Living and well 5 yrs. per cent	Living and well 5–13 yrs. per cent	Average survival of those dead of disease years
No metastases to axillary lymph nodes	81	85	76	4.7
Metastases involving less than half the axillary lymph nodes	22	68	50	4.6
Metastases involving more than half the axillary lymph nodes	31	38	22	3.4
Metastases involving all axillary lymph nodes	37	19	16	2.2
Total with metastases to axillary lymph nodes	90	38	28	3
Total	171	60	50	3.3

tion has been done to determine whether tumor susceptibilities in mice besides mammary carcinoma are transferred through breast milk. The results have been negative. There is no evidence of any kind even to suggest that the milk factor is in any way applicable to the human. Surveys are now under way at the University of Minnesota and the University of Ohio which, in a decade, may give us some light on this possibility. Although not directly inducing the disease, the possibility of the milk factor being a virus has greatly revived and stimulated interest in the virus theory of tumors. With the new electron microscope and the recently developed ultraviolet lighting method (Caspar of Sweden), amazing and beautiful pictures have been made from thin tissue cultures showing not only cell fission and mitosis but clearly showing the virus in the cell protoplasm. By these methods, virus has been demonstrated clearly in the cells of chicken sarcoma, in the large papillomas of the Western cotton tail rabbit and in the cells of hypernephroma to which the leopard frog of the marshes is so susceptible.

TABLE III.—RELATION OF LYMPH NODE METASTASES TO RECURRENCES IN THE OPERATIVE SCAR*

Cases	Metastases to axillary lymph nodes per cent	Recurrences in operative scar per cent
81	0	7
22	under 50	9
31	over 50	19
37	100	21

*Tables II and III appeared as Tables I and II in article by Shields Warren and V. N. Tompkins, Surg. Gyn. Obst., 1943, 73: 327–330.

TREATMENT

In the treatment of breast cancer, radical operation holds first place. The percentage of 5 year cures and the duration of life of those not cured are inversely proportional to the percentage of node involvement (Tables II and III). This is the most significant single fact for consideration in the therapy of breast cancer and the fact that makes the thorough, meticulous, systematized radical dissection of paramount importance.

For the past 24 years in my breast clinics, it has been my custom to count the nodes removed, to determine the percentage of malignant involvement and note their location. The radical operation is done in such a way that the layers of fascia can be spread out in sheets, and the nodes counted by hand lens and palpation, by the pathologist. The layers are numbered and the number of nodes, per cent involved, and location are included in the pathologist's report. This we have found not only of definite prognostic value but a practical guide in the after care and follow up of individual cases.

Every now and then all of us are confronted in consultation or in conference by a medical man or a surgeon who states that the radical operation is unnecessary, that just as good results can be obtained with simple mastectomy plus x-ray therapy. This statement should be immediately challenged and vigorously refuted. To accept it is to set breast surgery back more than 80 years to the time before Charles Hewitt Moore (the father of modern breast surgery). The facts are that x-ray will sterilize the breast in only one-third—33 per cent. When cancer is confined to the breast the radical operation gives 70 to 80 per cent 5 year cures. X-ray will sterilize involved axillary nodes only in 1 out of 4—25 per cent. The results of radical operation in those cases with axillary node involvement is 48 per cent 5 year cures. At present, radical operation certainly represents our best and most reliable means of combating this disease and whatever disrepute has fallen upon it is most often due to the hurried incomplete performance of it. There is no

other operation in surgery in which the result is so directly measured by a knowledge of the anatomy and by the thoroughness and precision of its performance.

X-ray and radium are purely ancillary and in no way competitive in the therapy of mammary carcinoma. Cancer of the breast is not radiosensitive nor radioresponsive. All breast cancers (except anaplastic) are radioresistant. Preoperative x-ray therapy has been generally abandoned. It did not add to the 5 year "cures." It greatly increased the blood loss during the radical operation because of perivascular fibrosis, which condition also interfered with the thoroughness of the dissection. Also, the incidence and degree of lymphedema of the arm was greatly increased by it. As for postoperative x-ray therapy, too much has always been expected of it by too many. It is not a substitute for, nor an excuse for, an incomplete radical dissection. There are three schools of thought regarding postoperative x-ray therapy: (1) those who do not advise it at all, (2) those who advise its use only when axillary nodes are found involved, and (3) those who employ it routinely.

All of these groups are composed of both roentgenologists and surgeons, sometimes one leading and the other following and vice versa. The first group says in substance, "If the radical operation has been well done what is there to treat? It is like shooting at the hole before the rat pokes his head out, etc." The answer to this group is one word—"implants." It has always been my contention that local recurrence in scar or skin flaps is due to implantation of cancer cells by the operator during the operation. By using an antiseptic technique, thin skin flaps and postoperative x-ray therapy, we have been able to reduce our local recurrences to less than 1 per cent. As high as 27 per cent have been reported in some clinics. The second group—those who advise postoperative x-ray therapy only when axillary nodes are involved—apparently presuppose that all the nodes were possibly not removed. It is rare for experienced surgeons to leave nodes and one rarely sees recurrence in the axilla among experienced operators. This policy would seem to shift some of the responsibility from the surgeon—where it all should remain, and on the other hand could possibly be an excuse for a less meticulous radical dissection. We have all heard surgeons say, "If there is any cancer left the x-ray will take care of it." If carcinoma is left in lymph nodes, and only 25 per cent can be sterilized by x-ray, no one should depend on that. As for the third group, those who advise routine postoperative x-ray therapy, it is unfortunate that a standard rational basis for this plan has not been agreed upon and advocated. I have, for many years, advised routine postoperative x-ray therapy on the basis that we can and often do accomplish two desiderata; i.e. destroy implanted cancer cells thereby avoiding or reducing local recurrences; second, destroy cancer cells already seeded in the mediastinal pathway en route to hilar nodes and lungs. On this basis we have advocated two different plans of treatment. Believing that implantation can arise only from two possible sources, the biopsy site, or from the nodes if they are involved, and that seeding into the mediastinal lymphatics can occur with or without node involvement, the plan of treatment is varied according to presence or absence of nodes, and in both plans of treatment deep therapy to the mediastinum is included. If no nodes are involved, a superficial soft tissue technique is mapped out, using four portals: axillary, suprascapular and upper incision, middle and lower part of incision, mediastinum. To the first three fields are given, tangentially, 200 roentgens each time, six times to each field, a total of 1200 rat units to each. The factors are 140 kilovolts, 3 millimeters aluminum, 50 centimeter target distance, 15 by 15 centimeter portals, 20 milliamperes 5½ seconds. To the mediastinal pathway deep therapy is given alternating with the other ports and using for the mediastinum 200 to 220 kilovolts, 312 rat units per treatment, 50 to 60 centimeter target distance, 0.5 to 1 millimeter copper filter every fifth day up to about 2100 roentgens.

In the group with node involvement the usual fractionated deep therapy is given, using 5 portals: suprascapular, axillary, breast area and center of scar, lower incision, mediastinum. The same factors and dosage are used to each of these portals as is given to the mediastinum as noted above.

In the treatment of inoperable carcinoma of the breast, simple mastectomy, x-ray therapy, and testosterone are our mainstays—simple mastectomy to avoid or get rid of a foul sloughing mass and improve the patient's condition and morale; x-ray and testosterone for palliation. It is amazing what can be done in relief and prolongation of life, and here, x-ray therapy really comes into its own, and most of us frequently find ourselves with a few of our "inoperables" comfortably outliving some of our 5 year "cures."

Castration in the therapy of breast cancer has much more historical interest than practical value. The most that can be said for it is that it has slight temporary effect for a short time in a few cases. In fact, the effect of castration is slight and inconsequential compared to the involution caused by cessation of lactation. But ever so often, since Schinzinger suggested castration for breast cancer in 1889 and since its performance in 8 cases by Beatson in 1896, it has been revived, tried and abandoned, again and again. All the statistical evidence, by a comparison of series, large and small, with and without castration, shows it to be of little or no value. If it has any value at all, it is in cases of diffuse and advanced bone metastases with high alkaline serum phosphatase. X-ray and testosterone, however, will do more for these cases than x-ray and castration. Castration has been advocated to prevent pregnancy, to protect the remaining breast, to prevent local recurrences and distant metastases. Pregnancy can be satisfactorily controlled with modern contraceptives. Tubal ligation is justifiable if other methods are objectionable. Surely no woman who has had a radical operation or other treatment for breast cancer should be allowed to become pregnant. The fate of the remaining breast is largely in the hands of the surgeon who does the radical operation. If he removes all the presternal fascia and destroys the superficial transmammary pathway the remaining breast is safe because this is the only direct lymphatic connection. Remembering that 2 per cent of breast cancer is initially bilateral, and that 5 per cent will become bilateral, this is an important consideration. As for local recurrences, they can to a large extent be avoided, and as for distant metastases, they have usually been seeded before operation, although not demonstrable by examination or x-ray. Postoperative x-ray therapy, especially to the mediastinum, is our only defense. In the middle 1930's, when x-ray therapy was having its revival in the treatment of breast carcinoma, both in the Scandinavian clinics and in the United States, castration by x-ray was added to the preoperative therapy. This entire plan has been discarded having been found to be of no help and to have many disadvantages.

In cancer of the male breast, castration is much more beneficial and the results far more striking. In fact the male, having no such compensatory gonadal mechanism, the results are comparable to or even surpass those seen in carcinoma of the prostate. In all advanced breast cancer in the male, especially with bone metastases, it is a valuable addition to the therapy.

Carcinoma of the breast during pregnancy presents a serious and often hazardous problem. The changes in the breast preparatory to lactation, the enormous increase in glandular and ductular elements, the increased blood supply and the increased stimulation, both by estrin and prolactin, all make for rapid fulminant growth. Also, the type and grade of cancer is usually duct or adenocarcinoma, grade 2 or 3. This fact adds to the rapid advance. No progress can be expected in the arrest or treatment of the breast lesion while the pregnancy exists. If it is less than 5 months and the breast lesion is still operable, the pregnancy should be interrupted at once, testosterone given daily in large doses, and the radical operation with adequate transfusions should be done as soon as the patient's condition permits. If the pregnancy is beyond 5 months and the breast lesion operable, hysterotomy, tubal ligation, transfusions and radical operation should be the plan. Testosterone will be of great value, but castration should be avoided because it will destroy the balance between estrin and prolactin and the resultant pituitary ascendancy will increase lactation or the preparation therefor.

In the late weeks of pregnancy, if the breast lesion is operable, cesarean section with an attempt at a viable child should be followed as

soon as possible with the radical operation, transfusions, testosterone, etc. If the lesion is frankly inoperable, a week or two of added fetal maturity may be permissible, the delivery to be followed by simple mastectomy, testosterone, and x-ray therapy. Each case should be carefully analyzed and individualized, the question of operability and the saving of the mother by the radical operation being the primary consideration, and the question of a viable child coming into first consideration only in the late weeks or in the obviously inoperable.

Special problems in the therapy of mammary carcinoma are also presented by Volkmann's inflammatory carcinoma (mastitis carcinosa), anaplastic carcinoma of the breast, and perhaps by duct carcinoma in young women.

In mastitis carcinosa, the brawny red edematous erysipeloid lesion not only spreads rapidly along the superficial lymphatics but quickly penetrates the breast through the interlobular lymphatics to involve the pectorals and fascia. Growth and penetration are usually so rapid that the lesion is soon beyond the hope of surgery which spreads the disease and hastens the end, the average duration of life being 6 to 8 months. The widespread involvement often results in cancer *en cuirasse*. If seen early the best palliative procedure is interstitial radiation, the so called radical radium needling (Keynes pattern).

Anaplastic carcinoma of the breast is often badly handled surgically with poor results. By the time the nodule reaches palpable size bone metastases have occurred in many instances, but fortunately both the primary lesion and the bone metastases are highly radiosensitive and radiotherapy is the treatment of choice. This is the only radioresponsive breast lesion.

Duct carcinoma in young women deserves special mention because of the pessimism and defeatist attitude regarding mammary cancer in the young. For this attitude there is no basis. Only 2 per cent of breast carcinoma occurs before 30 years or age and the best results of radical operation are obtained from 35 to 50 years of age. The points that should be stressed in the younger group are two: This is the age of active cyclic changes in the breast, and of fibrocystic disease, and these women are more likely to become victims of cancer. Second, young women with active breasts usually develop one of the more rapidly growing types of cancer—adenocarcinoma or duct carcinoma, grading 2 or 3—and not scirrhus. Early diagnosis is imperative, but while still operable the results compare favorably with the same type and grade in the older group. If testosterone has any place in prophylaxis against recurrence after radical operation, it is in these young women with grade 2 or 3 growths. Castration *should be avoided*. It will give the whip hand to the pituitary by removing its biologic antagonist, estrin. Prolactin, the luteotrophic hormone of the pituitary, is much more to be feared. Testosterone will suppress it most satisfactorily.

CAUSES OF FAILURE

Although the facts and figures definitely justify an optimistic realism in the problem of breast carcinoma, it is always of value and interest to review our causes of failure critically.

1. Late diagnosis. Early diagnosis will alone save 4,000 additional lives in the United States each year (Fig. 5).

2. Failure to recognize inoperability, as follows: (a) supraclavicular nodes; (b) fixation of axillary nodes; (c) fixation of the breast on chest wall; (d) distant metastases, to lung, liver, bones; (e) widespread parietal dissemination—diffuse secondary subcutaneous nodules; (f) mastitis carcinosa, Volkmann's inflammatory carcinoma; (g) cancer *en cuirasse;* (h) anaplastic carcinoma; (i) incurable constitutional diseases which may lead to fatality. This is particularly in the aged group, cardiac, cardiorenal, etc. in which the radical operation would be hazardous, and the life expectancy with simple mastectomy would equal that of the complicating disease.

Under inoperability we should frankly discuss the one most discouraging feature of breast surgery, the factor which I have, for many years, called "*preseeding*" to emphasize its importance to my graduate students. We have found in our follow up clinics, that, in spite of careful preoperative examination which routinely includes an x-ray survey of chest, spine, ribs and pelvis, in 11 per cent of

our cases the patient returns within 2 years with a distant metastasis which must have been seeded prior to the radical operation. This *preseeding* gives no clue whatever of its existence either in symptoms, physical signs, or x-ray evidence. Its possibility always exists. The more advanced the lesion, the greater the percentage of node invasion, the more of a possibility it becomes. It can and does occur without axillary node involvement although infrequently. This is not surprising if we recall that 4 of the 8 pathways of spread do not traverse the nodes (mediastinal, transmammary, epigastric, superficial abdominal). The discouraging feature is that we are almost defenseless against *preseeding*. Our only defense is x-ray therapy to the mediastinum, as a part of our routine postoperative program. All 4 of the other "outside" pathways are included in the x-ray therapy fields as a routine measure.

3. Inadequate and incomplete radical operation: Unfortunately some surgeons, although skilled in their fields, seem to regard the radical breast dissection as just another operation, a task to be quickly completed. Speed has no place in this work. Others, engrossed in anatomical and technical detail, take no precaution whatever against implantation. Unless one is cancer cell minded disastrous consequences follow. Other common errors of technique are failure to remove the superficial fascia from the skin flaps and to remove the epigastric and subscapular node groups.

4. Pessimism and defeatism, as a cause of failure, are not justified by the facts and figures and are too often due to a lack of knowledge of them. There is no place in breast surgery for the defeatist and nothing to support him.

SUMMARY

Although cancer of the breast is increasing annually, the cure rate is increasing more rapidly than the incidence. "Fight Cancer with Knowledge" can be applied to the medical profession as well as to the laity. Nowhere in the realm of surgery is it so true that "Knowledge is Power" as it is in breast cancer, and in this instance, it often means power to save lives.

LABORATORY AND CLINICAL EXPERIENCES WITH STREPTOMYCIN THERAPY IN THE MANAGEMENT OF INFECTIONS OF INTESTINAL ORIGIN

HENRY L. SILVANI, M.D., SANFORD ROTHENBERG, M.D., HELEN WARMER, A.B., JOYCE AMLUXEN, A.B., and H. J. McCORKLE, M.D., San Francisco, California

DURING the past 6 months careful clinical and laboratory studies have been made on 13 patients with serious intra-abdominal infections who have received streptomycin therapy (Table I). Five were patients with acute diffuse peritonitis; 6 had intra-abdominal abscesses; 1, acute cholangitis; and 1, an abscess of the liver. Streptomycin was given by intramuscular injection at 3 hour intervals in all cases. The patients with diffuse peritonitis each received from 24 to 52 grams of streptomycin over periods of 8 to 14 days (2.7 to 4 grams daily). The other patients each received from 15 to 48 grams of streptomycin over periods of 5 to 16 days (3 to 4 grams daily). Other chemotherapy was discontinued during the period of treatment with streptomycin in all except 2 cases, in which penicillin and streptomycin were given concurrently. Since most of these patients were seriously or critically ill with infection, they received, in addition to the chemotherapy, supportive fluids and transfusions, continuous aspiration of the stomach and upper intestinal tract when necessary, and surgical procedures for removal or drainage of septic foci when indicated.

CASE 1. After an acute illness of 30 hours' duration, a woman 23 years of age was found to have a diffuse peritonitis originating from a gangrenous perforated appendix. Appendectomy with drainage of the abdominal wound was done. Bacteria cultured from the peritoneal exudate were Escherichia coli and beta hemolytic streptococci. These organisms were susceptible *in vitro* to 4 to 5 units of streptomycin per cubic centimeter (a concentration within the blood streptomycin level obtained with the dosage used). Streptomycin therapy was started immediately after operation. The patient received 24 grams of streptomycin over a period of 9 days (2.7 grams daily). The patient convalesced satisfactorily. She became afebrile on the 6th postoperative day and the wound healed without infection by the 14th postoperative day. It is possible but doubtful that streptomycin therapy contributed to the recovery of this patient.

CASE 2. After an acute illness of 36 hours' duration, a man 18 years of age was found to have a diffuse peritonitis originating from a gangrenous perforated appendix. Appendectomy was performed. Bacterial cultures made from the peritoneal exudate contained Escherichia coli and staphylococci (type). *In vitro* these organisms were resistant to streptomycin in concentrations up to 150 units per cubic centimeter (a concentration considerably above the blood levels obtainable with the dosage and method of administration used). The patient received 23.4 grams of streptomycin over a period of 8 days (3 grams daily). All symptoms of diffuse peritonitis subsided rapidly. The patient was afebrile by the 5th postoperative day and the abdominal wound healed without infection in 12 days. It appears unlikely that streptomycin contributed to recovery in this case.

CASE 3. A man 67 years of age gave a history of lower abdominal pain of 15 hours' duration, and showed signs of peritonitis. Laparotomy revealed a perforated diverticulum of the sigmoid colon and diffuse peritonitis. Three hours after operation streptomycin therapy was started. He received 27 grams (2.7 grams daily) over a period of 10 days. Unfortunately, the culture tube was broken, so that bacteriological data could not be obtained. Postoperatively the patient remained acutely ill and febrile, and the laparotomy incision became infected. After 10 days streptomycin therapy was discontinued, and penicillin and sulfonamide therapy started. Within 12 hours after therapy was changed the patient was afebrile. Obviously streptomycin therapy was of no value in this case.

CASE 4. An elderly woman was acutely ill for 16 days with generalized abdominal pain, vomiting, and jaundice. Chemotherapy with penicillin and sulfadiazine had no appreciable effect on the course of her illness. She appeared moribund. Streptomycin therapy was started, 4 grams daily being given. After 24 hours of streptomycin treatment the patient's condition improved remarkably and an operation was performed. A diffuse peritonitis due to perforation of the common bile duct by a calculus was found. Bac-

From the Department of Experimental Surgery of the University of California Medical School. This project received financial support from the Christine Breon Fund. Presented in the Forum on Fundamental Surgical Problems before the Clinical Congress of the American College of Surgeons, December, 1946.

TABLE I.—CLINICAL USE OF STREPTOMYCIN

Case	Diagnosis	Source of infection	Bacteriology	Amount of streptomycin gm.	Effects of streptomycin
1	Diffuse peritonitis	Perforated acute appendicitis	Escherichia coli, beta hemolytic streptococcus	24	Doubtful, but possibly beneficial
2	Diffuse peritonitis	Perforated acute appendicitis	Escherichia coli, staphylococcus type undetermined	23.4	Doubtful
3	Diffuse peritonitis	Sigmoid diverticulitis	No cultures obtained	27	Of no value
4	Diffuse peritonitis	Perforated common bile duct	Escherichia coli, proteus vulgaris, streptococcus fecalis	36	Probably beneficial
5	Diffuse peritonitis	Perforated amebic ulcer of colon	No cultures obtained	52*	Possibly beneficial
6	Abdominal abscess (pelvic)	Colon resection with anastomosis	No cultures obtained	24	Of no value
7	Abdominal abscess	Colon resection with anastomosis	Escherichia coli, beta hemolytic streptococcus, alpha hemolytic streptococcus	33	Of no value
8	Abdominal abscess	Regional ileitis	Escherichia coli, streptococcus viridans, clostridium welchii	36	Doubtful
9	Abdominal abscess	Sigmoid diverticulitis	Escherichia coli, nonhemolytic staphylococcus	30	Doubtful
10	Abdominal abscess	Pelvic inflammatory disease	Escherichia coli, nonhemolytic staphylococcus albus, alpha hemolytic streptococcus	48	Of no value
11	Abdominal abscess (pelvic)	Repair of rectovaginal fistula	Hemolytic staphylococcus albus	42	Doubtful, but possibly beneficial
12	Acute cholangitis	Common bile duct stricture	No cultures obtained	15*	Doubtful
13	Hepatic abscess	? Hematogenous	Beta hemolytic streptococcus, Bacterioides	24	Doubtful

*Combined with penicillin therapy.

teriological cultures made from the peritoneal exudate showed the presence of Escherichia coli, Proteus vulgaris, and Streptococcus fecalis. *In vitro* laboratory determinations indicated that the Escherichia coli and Streptococcus fecalis were susceptible to concentrations of 40 units of streptomycin per cubic centimeter, and the Proteus vulgaris was susceptible to 20 units of streptomycin per cubic centimeter. A total of 36 grams of streptomycin was given over a period of 9 days. The patient recovered. Streptomycin therapy probably was beneficial in this case.

CASE 5. A woman 35 years of age had been ill with amebic colitis for 3 weeks when she suddenly developed severe abdominal pain and signs of diffuse peritonitis. It was believed that she had a perforation of an amebic ulcer of the colon. She had been acutely ill with peritonitis for 5 days and appeared moribund before antibiotic therapy was started. No cultures were obtained. She received 4 grams of streptomycin and 400,000 units of penicillin daily for 14 days. She improved slowly and recovered. Streptomycin therapy may possibly have been of some value in this case.

CASE 6. A woman 40 years of age developed a pelvic abscess after resection and anastomosis of the pelvic colon. She was febrile and acutely ill for 15 days before streptomycin therapy was begun. She received 3 grams of streptomycin daily for 8 days, a total of 24 grams, without apparent benefit. After a colostomy and surgical drainage of the abscess were done, she recovered rapidly. Streptomycin therapy obviously had no effect in this case.

CASE 7. A 66 year old man developed an abdominal abscess with a draining wound 3 months after resection and anastomosis of the colon. Cultures contained Escherichia coli (susceptible to 7.1 units of streptomycin per cubic centimeter), beta hemolytic streptococcus (susceptible to 2.5 units of streptomycin per cubic centimeter) and alpha hemolytic streptococcus (susceptible to 0.2 unit per cubic centimeter). He had been ill for 2 months when streptomycin therapy was instituted. He was given 3 grams of streptomycin daily for 11 days (a total of 33 grams) without apparent benefit.

CASE 8. A 25 year old woman had been ill with regional ileitis for 7 years. An operation was performed for resection of the diseased intestine and drainage of abdominal abscesses. Bacterial cultures demonstrated Escherichia coli, Streptococcus viridans, and Clostridium welchii. Streptomycin therapy was started on the first postoperative day. Four grams of streptomycin were given daily for 9 days (a total of 36 grams). The patient became afebrile in 3 days. Wound drainage diminished rapidly, and the wound closed in 10 days. It is doubtful that streptomycin contributed to recovery in this case.

CASE 9. A man 44 years of age was found, on exploratory laparotomy, to have an abdominal abscess associated with diverticulitis of the sigmoid colon. Six months later the abscess was still present, and

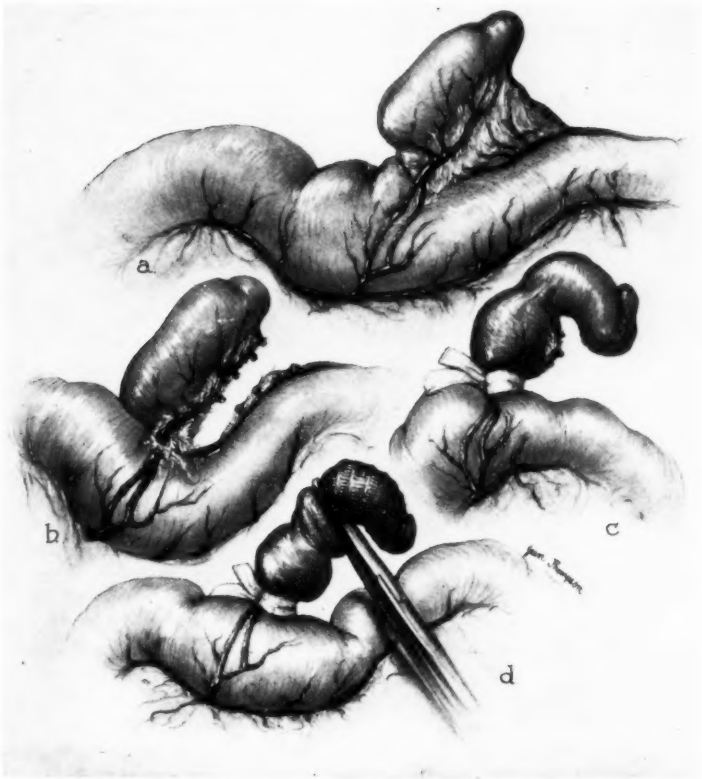


Fig. 1. Diagram indicating method of producing diffuse experimental peritonitis of appendiceal origin. The vascular supply is divided, the base of the appendix is ligated, the appendix is crushed, and the spleen and omentum are removed.

there was purulent drainage from the laparotomy wound. Bacterial cultures contained Escherichia coli (susceptible to 28.5 units of streptomycin per cubic centimeter) and a nonhemolytic Staphylococcus aureus (susceptible to 20.0 units of streptomycin per cubic centimeter). He was given 3 grams of streptomycin daily for 10 days (a total of 30 grams). During this course of treatment the patient's condition improved and the drainage from the wound ceased. However, this result must be considered to be doubtful because the patient had previously had many similar remissions with temporary closure of the wound.

CASE 10. A 25 year old woman had been acutely ill with tubo-ovarian abscesses for 4 months. In spite of two operations for drainage of abscesses she remained acutely febrile and became progressively worse. Cultures made from the abscesses contained Escherichia coli, nonhemolytic Staphylococcus albus, Pseudomonas aeruginosa and alpha hemolytic streptococcus. She was treated with 3 grams of streptomycin daily for 16 days (a total of 48 grams). The Escherichia coli and Pseudomonas aeruginosa disappeared from her cultures, but the clinical course of the disease continued progressively downhill. Streptomycin therapy did not help in this case.

CASE 11. A woman 48 years old developed a pelvic peritonitis and abscess after repair of a rectovaginal fistula. Bacterial cultures contained hemolytic Staphylococcus albus. She had been acutely ill and febrile for 14 days before streptomycin therapy was started. She received 3 grams of streptomycin daily for 14 days (a total of 42 grams). Her temperature dropped from 103 degrees F. to normal during streptomycin therapy. Streptomycin therapy may have been helpful in this case, but it is doubtful.

CASE 12. A man 47 years of age had a history of many episodes of acute cholangitis following an operation for removal of stones from the common bile duct. He entered the hospital with an attack of up-

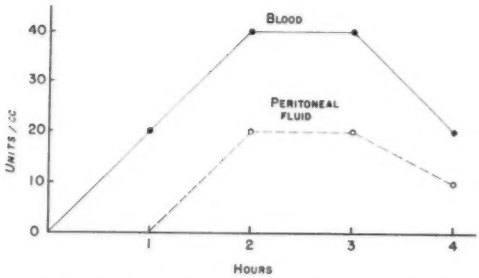


Fig. 2. Blood and peritoneal streptomycin levels following a single intramuscular dose of 0.33 gram of streptomycin (dog).

per abdominal pain, chills, fever (40° C.) and icterus, of 48 hours' duration. Blood cultures produced no bacterial growth. Penicillin therapy was given for 1 day pending the arrival of streptomycin. On the third day of his illness, a few hours after his temperature had subsided to normal, streptomycin therapy was started. He received 3 grams of streptomycin daily for 5 days (total amount 15 grams). The patient recovered completely from this attack of cholangitis, but improvement began a few hours before streptomycin therapy was started; therefore, its value in this case must be considered as doubtful.

CASE 13. A man 48 years of age had been ill for 2 months with chills, fever, sweats, and upper abdominal pain. An abscess of the liver was drained and bacterial cultures of the pus contained beta hemolytic streptococcus and Bacterioides. (*In vitro* tests indicated resistance of these organisms to streptomycin in concentrations as high as 2,000 units per cubic centimeter.) After drainage of the abscess, the patient was given 3 grams of streptomycin daily for a period of 8 days (a total of 24 grams). The Bacterioides soon disappeared but the streptococcus persisted for some time in the cultures. The patient recovered completely. It appears doubtful that streptomycin therapy was helpful in this case.

TABLE II.—STREPTOMYCIN SUSCEPTIBILITY OF BACTERIA CULTURED FROM PERITONEAL EXUDATE OF ANIMALS WITH EXPERIMENTAL PERITONITIS OF APPENDICEAL ORIGIN

Organism	Effective concentration of streptomycin (units/c.c.)
Escherichia coli	1.78–20.0
Proteus vulgaris	7.1–80.0
Bacterioides	Not susceptible
Aerobic sporeforming bacillus	3.0
Pseudomonas aeruginosa	Not susceptible
Clostridium	Not susceptible
Alpha hemolytic streptococcus	Most strains not susceptible
Beta hemolytic streptococcus	1.3–28.5
Gamma streptococcus	3.57
Streptococcus fecalis	Not susceptible
Nonhemolytic staphylococcus albus	3.57–80.0
Hemolytic staphylococcus albus	14.6
Hemolytic staphylococcus aureus	3.0–8.0

TABLE III.—EXPERIMENTAL PERITONITIS—UNTREATED CONTROL SERIES

Number of animals	10
Survived	0
Died	10
Average period of survival	39 hours

Bacteria cultured	Number of animals (Incidence)
Escherichia coli	10
Proteus vulgaris	1
Bacterioides	1
Clostridium	10
Alpha hemolytic streptococcus	3
Beta hemolytic streptococcus	1
Streptococcus fecalis	3
Nonhemolytic staphylococcus albus	5
Hemolytic staphylococcus albus	3

Necropsy findings: diffuse peritonitis in all animals

It was difficult to evaluate, from these clinical studies, the effect of streptomycin therapy on intra-abdominal infections. In order to obtain more information regarding the value of streptomycin, a group of surgical laboratory experiments was undertaken.

Fulminating diffuse peritonitis was produced in dogs by a modification of the method of Bower described previously (8). This consisted of dividing the blood supply to the appendix, ligating the base with umbilical tape, crushing the wall of the appendix and removing the omentum and spleen (Fig. 1), and administering 60 cubic centimeters of castor oil by gavage. All animals received supportive therapy consisting of parenteral fluids and electrolytes throughout the postoperative period. A small soft rubber tube was brought out through the abdominal incision, from which peritoneal fluid was withdrawn for bacterial cultures, and in two groups of animals streptomycin was instilled locally through these tubes. In most of the animals the tubes functioned satisfactorily but occasionally the animal would withdraw the tube before the experiment was completed. *In vitro* streptomycin susceptibility tests of bacteria cultured from the peritoneal exudate of animals with experimental peritonitis are shown in Table II. Thirty-five animals were used for the experiment. Ten served as untreated controls, 10 animals received systemic streptomycin therapy beginning 6 hours postoperatively, and 10 received local streptomycin

TABLE IV.—EXPERIMENTAL PERITONITIS—SYSTEMIC STREPTOMYCIN THERAPY BEGUN 6 HOURS POSTOPERATIVELY

Dosage—.33 gram of streptomycin intramuscularly every 4 hours—2.0 grams daily

Number of animals	10
Survived	1
Died	9*
Average period of survival	92 hours

*One animal developed a fecal fistula apparently after surviving the original period of acute diffuse peritonitis.

Bacteria cultured	6 hours postoperatively before therapy (7 animals) (Incidence)	At necropsy (9 animals) (Incidence)
Escherichia coli	6	9
Proteus vulgaris	0	0
Bacterioides	1	0
Aerobic sporeforming bacillus	1	1
Clostridium	5	8
Alpha hemolytic streptococcus	1	1
Beta hemolytic streptococcus	2	4
Gamma streptococcus	2	1
Streptococcus fecalis	1	2
Nonhemolytic staphylococcus albus	2	2
Hemolytic staphylococcus albus	1	1
Hemolytic staphylococcus aureus	1	1

Necropsy findings: Diffuse peritonitis in all animals that died

therapy. The animals receiving systemic streptomycin therapy were given 2 grams of streptomycin daily (.33 gram every 4 hours) by the intramuscular route. Figure 2 shows relative blood and peritoneal streptomycin levels following a single intramuscular dose of 0.33 gram of streptomycin.

All of the 10 untreated control animals died with diffuse peritonitis. The average period of survival was 39 hours. The organisms cultured from the peritoneal fluid of the untreated control series are shown in Table III.

Of the group of 10 animals that received systemic streptomycin therapy beginning 6 hours postoperatively, 9 died and 1 survived. One of the animals that died apparently survived the period of acute diffuse peritonitis but developed a fecal fistula with overwhelming infection. The average period of survival of the animals that died with diffuse peritonitis was 3 days 20 hours. It is interesting that the bacterial organisms cultured from the peritoneal fluid 6 hours after the onset of peritonitis generally were the same types and in roughly similar proportion to those cultured from the peritoneal fluid at necropsy (see Table IV).

TABLE V.—EXPERIMENTAL PERITONITIS—SYSTEMIC STREPTOMYCIN THERAPY BEGUN IMMEDIATELY POSTOPERATIVELY

Dosage—.33 gram of streptomycin intramuscularly every 4 hours—2.0 grams daily

Number of animals	5
Survived	0
Died	5
Average period of survival	75 hours

Bacteria cultured	6 hours postoperatively (4 animals) (Incidence)	At necropsy (5 animals) (Incidence)
Escherichia coli	2	3
Bacterioides	0	1
Clostridium	3	4
Alpha hemolytic streptococcus	0	1
Beta hemolytic streptococcus	1	0
Gamma streptococcus	1	0
Streptococcus fecalis	2	3
Nonhemolytic staphylococcus albus	2	0
Nonhemolytic staphylococcus aureus	1	0
Diphtheroid bacillus	2	0

Necropsy findings: Diffuse peritonitis, all animals

All of the 5 animals that received systemic streptomycin therapy beginning immediately after the operation to produce diffuse peritonitis died. The average period of survival was 3 days 3 hours and the bacterial cultures from the peritoneal fluid 6 hours after operation were roughly similar to those made from the peritoneal fluid at necropsy (see Table V).

TABLE VI.—EXPERIMENTAL PERITONITIS–INTRAPERITONEAL STREPTOMYCIN (NO SYSTEMIC THERAPY GIVEN)

Dosage—0.4 gram of streptomycin given intraperitoneally twice daily the first postoperative day and once daily thereafter

Number of animals	5
Survived	0
Died	5
Average period of survival	87 hours

Bacteria cultured	Hours postoperative (4 animals)					Necropsy (5 animals)
	6 hours	22 hours	30 hours	48 hours	72 hours	
	(Incidence)					
Escherichia coli	2	0	0	1	2	4
Clostridium	3	3	4	4	4	5
Alpha hemolytic streptococcus	2	0	1	0	1	4
Gamma streptococcus	0	0	0	0	0	1
Streptococcus fecalis	1	0	2	1	1	0
Nonhemolytic staphylococcus aureus	2	2	2	0	0	1

Necropsy findings: Diffuse peritonitis

All animals receiving systemic streptomycin therapy were acutely ill and toxic. Their appearance was identical with that of the untreated control animals.

Five animals received 0.4 gram of streptomycin intraperitoneally (through a small rubber tube), twice on the day of operation and once daily thereafter. All 5 animals died of diffuse peritonitis. The average period of survival was 3 days 15 hours. The bacterial flora was not significantly altered by this therapy (see Table VI).

Five animals received intraperitoneal instillations of 4.0 grams of streptomycin beginning immediately after operation, twice on the day of operation and at 24 hour intervals thereafter. Bacterial cultures made after a period of 6 hours and again at necropsy indicated that doses of 4.0 grams intraperitoneally effectively sterilized the peritoneal fluid in 4 of 5 animals. Cultures of the peritoneal fluid of the remaining animal showed the presence of Escherichia coli and Clostridium welchii. However, animals treated with such large doses of streptomycin intraperitoneally invariably died of streptomycin intoxication with respiratory failure, apparently of central origin.

SUMMARY

A group of 13 patients with serious intra-abdominal infections was treated with systemic streptomycin therapy. The result of streptomycin therapy was believed to be probably beneficial in 1 case, possibly beneficial in 1 case, doubtful but possibly helpful in 2, of doubtful value in 5, and of no value in 4 cases.

In a series of animals in which fulminating diffuse peritonitis of appendiceal origin was produced, systemic and local streptomycin therapy in dosages used apparently prolonged the lives of the animals, but did not significantly alter the bacterial flora of the peritoneal exudate or save the lives of the animals.

REFERENCES

1. Bower, John O., Burns, John C., and Mengle, Harold A. Surg. Gyn. Obst., 1938, 66: 947–961.
2. Idem. Surgery, 1938, 3: 645–657.
3. Epps, C. H., Ley, E. B., and Howard, R. M. Surg. Gyn. Obst., 1942, 74: 176–179.
4. Fauley, G. B., Duggan, T. L., Stormont, R. T., and Pfeiffer, C. C. J. Am. M. Ass., 1944, 126: 1132.
5. Kay, John H., and Lockwood, John S. Surgery, 1946, 20: 56–71.
6. Murphy, John J., Ravdin, Robert G., and Zintel, H. A. Surgery, 1946, 20: 445–451.
7. Pulaski, E. J., and Spinz, H. Ann. Surg., 1947, 125: 194–202.
8. Rothenberg, Sanford, Silvani, H., and McCorkle, H. J. Surgery, 1947, 22: 550–551.

THE MICROSCOPIC CRITERIA FOR THE DIAGNOSIS OF EARLY CARCINOMA OF THE CERVIX UTERI

EUGENIA E. GURSKIS, M.D., DONALD C. BEAVER, M.D., and
HARRY M. NELSON, M.D., F.A.C.S., Detroit, Michigan

ONE of the first papers on early noninvasive carcinoma of the cervix uteri was written by Rubin and appeared in 1910. It contained the report of 3 cases in which the diagnosis was made by the presence of atypical cells and loss of cellular polarity confined to the surface squamous epithelium. This author reached the conclusion that the diagnosis of early carcinoma depended upon these microscopic cell changes and that a pathological diagnosis of cancer in the preclinical preinvasive stage was possible. Schiller, in 1933, described the early malignant changes of squamous epithelium of the cervix uteri as consisting of the presence of nuclei up to the surface of the epithelium, the presence of atypical and polymorphic cells especially as regards the nuclei, a sharply demarcated basal layer against the underlying connective tissue, and a distinct, oblique line of demarcation between the normal and carcinomatous cells. Meyer, in 1941, described these changes as an increase of nuclear chromatin, enlargement of nuclei, loss of regular layering, and a 45 degree angle at the junction between normal and carcinomatous tissue. Using epithelium of the skin, Broders previously, in 1932, had identified the changes of early carcinoma as consisting of an increase in size and irregularity of the cells, more basophilic nuclei, atypical mitoses, and occasional grouping of the cells as tumor giant cells. He found that invasion was not necessary for a diagnosis of malignancy.

SELECTION OF MATERIAL FOR STUDY

This study was made by obtaining the cervices from the microscopic slide files of the laboratory of Woman's Hospital over a period of approximately 10 years, and from the services of Dr. Mark Maun and Dr. Lawrence Berman of the department of pathology of Wayne University, College of Medicine, Detroit. Cervices numbering 4,054 were selected from the files of Woman's Hospital which revealed benign lesions including hypertrophy, hyperplasia, metaplasia, leucoplakia, parakeratosis, hyperkeratosis, polyps, lacerations, scars, ulcerations, erosions, cervicitis, endocervicitis, and so called precancerous changes of the cervix. The stratified squamous epithelium of the portio vaginalis was the particular point of study, since it is from this area that 95 per cent of all cervical carcinomas arise.

From the Departments of Gynecology and Pathology of Woman's Hospital, Detroit, Michigan.

METHOD OF STUDY

From these 4,054 cases, 7 were selected, containing early noninvasive carcinoma. Eight additional cases were obtained from other institutions for a total of 15 cases (Table I). Of these 15 cases, 6 of early noninvasive carcinoma also demonstrated early invasive carcinoma in other areas of the same cervix. These 6 cases were included in the study for comparison with the early noninvasive lesions.

The cervices were studied microscopically for changes in cell morphology of the surface stratified squamous epithelium specifically, compared with normal cervices or cervices revealing benign lesions. Paraffin section technique and hematoxylin-eosin staining were employed. The stage of early squamous cell carcinoma in the preclinical noninvasive stage is thus particularly emphasized. This stage of early carcinoma is referred to by some authors (3) as intraepithelial carcinoma or as carcinoma *in situ* by others (1). In this stage the changes were observed microscopically rather than grossly, and were present chiefly in the surface squamous epithelium. No clinical follow-up has been pursued to indicate the accuracy of the observations. Only microscopic comparison with early invasive carcinoma and

TABLE I.—ESSENTIAL PATHOLOGICAL DATA ON THE FIFTEEN CASES STUDIED

Case Number	Benign lesions	Dark oval nuclei	Cytoplasm decreased in amount	Non-distinguishable basal layer	Mitoses	Intact basement membrane	Line of demarcation	Lymphocytic infiltration (stroma)	Number of cells	Loss of polarity	Invasion	Changes in areas of metaplasia	Changes in areas of leucoplakia
1	Chronic cervicitis	1	1			+	Vertical	2	1	1			
2	Chronic cervicitis, erosion	2 & 3	3	+	2	+	Gradual	2	2	1			
3	Erosion, polyp, inflammation	2	3	+	2		Oblique	3	3	3	+		
4	Metaplasia	3	3	+	3	+		1	3	3		+	
5	Metaplasia, polyp, cyst, chronic cervicitis	3	3	+	2	+		2	3	3		+	
6	Metaplasia, leucoplakia cysts, ulcerations	3	3	+	3	+	Gradual	2	2	3			+
7	Metaplasia, erosion, hypertrophy, early metaplasia	2 & 3	3		2	+	Gradual	3	2	1		mild	
8	Pregnancy	2 & 3	3	+	3		Gradual	3	3	3	+		
9	Leucoplakia, bilateral lacerations, papillomas	3	3	+	2			2	2	3	+		+
10	Metaplasia, chronic cervicitis, hyperplasia	3	3	+	2		Oblique	3	2	3	+	+	
11	Metaplasia, lacerations, erosion, scar, hyperplasia, chronic cervicitis	3	3		2	+		2	2	3			
12	Metaplasia, polyp	3	3	+	3			2	3	3	+	+	
13	Metaplasia, erosion, chronic cervicitis	3	3	+	2	+		2	2	1		+	
14	Metaplasia, erosion, scars, nabothian cyst	3	3	+	2	+		3	2	3		+	
15	Metaplasia, lacerations	3	3	+	2			2	2	3	+	+	
	Totals	15	15	12	14	9	7	15	15	15	6	8	2

+designates that the condition indicated is present.
1—mild; 2—moderate; 3—marked.

stages of invasive or clinical carcinoma forms the basis of the study. The squamous epithelium of the portio vaginalis consists normally of two layers, namely, the stratum germinativum, several cells in thickness and the basal layer, one cell in thickness. The cells of the stratum germinativum are rather large and polyhedral, with round nuclei staining with a moderate intensity and with a considerable amount of cytoplasm. These cells are rather regularly spaced and appear to be in horizontal parallel rows. The more peripheral cells become somewhat flattened horizontally and appear larger and contain more cytoplasm. The cells of the basal layer are smaller than those of the stratum germinativum and contain a smaller amount of cytoplasm. The nuclei are small, round to oval, stained deeply, and the cells are placed parallel to one another, more or less perpendicular to the cells of the stratum germinativum.

DISCUSSION OF CASES

The most characteristic finding of the squamous epithelium, indicating departure from normal toward malignant transformation, was the presence of deeply stained (hyperchromatic), oval nuclei. This characteristic was always present and was diagnostic; however, it was found to exist to a varying degree. As a rule, the density of the nuclear stain was not as great in the earliest stages as exemplified by Case 1 (Fig. 1). Occasionally variations in the nuclear staining and size could be seen in the same cervix. For example, in Case 2 (Fig. 2) in one area the nuclei were deeply stained and large while in another area they were smaller and even darker stained. In Case 4 (Fig. 5) the nuclei appeared more or less uniformly oval and dark.

Decreased amount of cytoplasm in the epithelial cells was observed almost as often in frequency as the nuclear changes. This find-

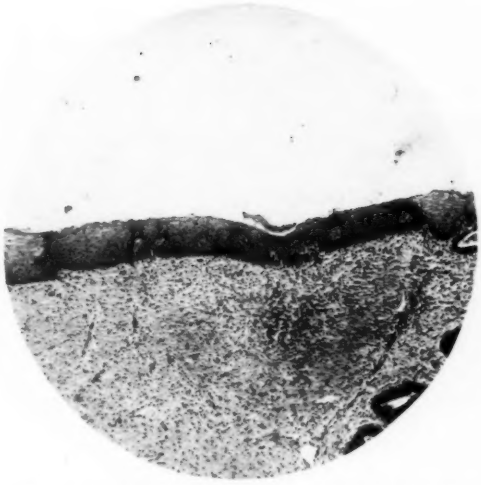


Fig. 1. Case 1. This case reveals an extremely early carcinoma of the cervix with abrupt demarcations from the normal epithelium on each side of the lesion. × 65.

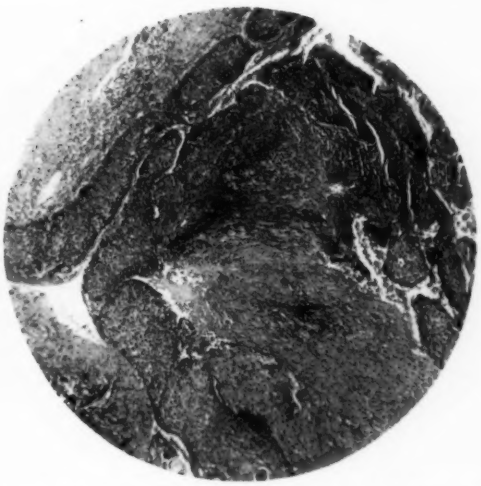


Fig. 2. Case 2. This case discloses several stages of early carcinoma in the same cervix, especially observed in the epithelium in the upper right. Epithelium of lower left is relatively normal. × 65.

ing was more pronounced in the advanced cases. In Case 1 (Fig. 1) the cytoplasm was mildly decreased in amount and was more marked in the cells nearest the basal layer. All the other cases revealed a marked decrease of cytoplasm in the epithelial cells.

Another important characteristic was the development of a nondistinguishable basal layer. This layer seemed to replace the upper layers so that all the cells appeared similar to the basal cells. Of the 15 cases presented, 12 cases disclosed this characteristic. The contrast between the basal layer of early carcinoma and normal epithelium can be seen in Case 3 (Fig. 4). In this microscopic section the normal epithelium had a single-cell basal layer; in the carcinomatous zone, there was an abrupt change and the basal layer was not distinguishable from the cells above. This characteristic was also present in the areas of metaplasia disclosing changes of early carcinoma. In Case 5 (Fig. 7) the squamous epithelial cells of the entire gland appeared similar and the basal layer was not distinguishable. This change was outstanding in this case as revealed by a comparison with the changes of metaplasia without the characteristics of early carcinoma. In Case 6 (Fig. 8) leucoplakia was present in the area associated with early carcinoma. Where leucoplakia was present alone, the basal layer was well defined and several cells in thickness. In the areas of early carcinoma in this section, the basal layer appeared indistinguishable from cells above it.

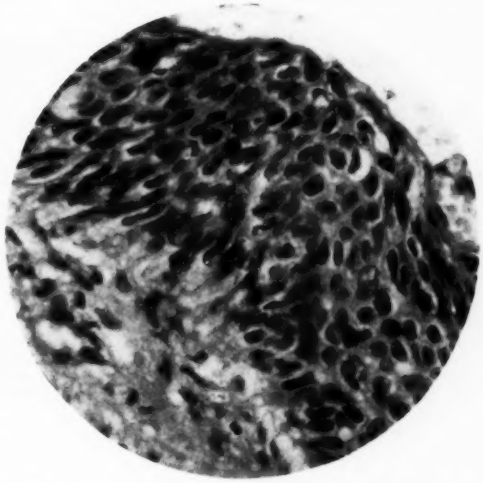


Fig. 3. Case 2. High power photomicrograph of the same case as Figure 2. Basal layer is indistinguishable in the areas of early carcinoma. × 395.

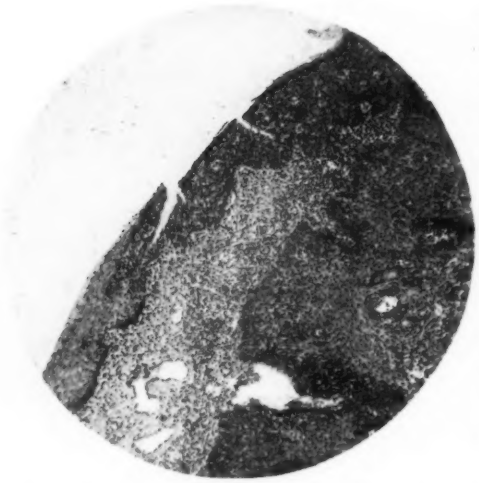


Fig. 4. Case 3. This case reveals the abrupt oblique line of transition between the early carcinoma and the normal epithelium (lower left of upper strip of epithelium). Other areas of this same cervix reveal invasive carcinoma. × 65.

Mitoses were found occasionally in 10 cases and to a marked degree in 4 cases. In Cases 4 (Fig. 6) and 6 (Fig. 8) may be seen numerous mitotic figures.

The presence of an intact basement membrane was also an important characteristic of early carcinoma and was diagnostic of the preinvasive stage. In the 6 cases which also contained invasive carcinoma, the basement membrane was penetrated in the areas of invasive carcinoma, even though it was intact in the areas of early carcinoma in the same cervix. In the 9 cases of early carcinoma alone, the basement membrane was intact. Case 8 (no illustration) revealed both conditions in different areas. An intact basement membrane was also seen in the areas of metaplasia associated with early carcinoma as disclosed in Case 5 (Fig. 7).

The line of demarcation between the carcinomatous and the normal epithelium was searched for and was identified in 7 of the 15 cases. In 3 of these the demarcation was sharp and in 4, it was gradual. Case 1 (Fig. 1) disclosed a demarcation on both sides of the area involved. In Case 3 (Fig. 4) the demarcation was very definite and was an oblique line. In Case 2 (Fig. 2) the transition from normal epithelium to carcinomatous epithelium was gradual. At the upper part of the photomicrograph the cells of the epithelium appeared normal, then there was an increase in thickness of the cells of the basal layer. The photomicrographs for Case 7 (no illustration) and Case 8 (no illustration) also revealed gradual transitions.

The stroma underlying the carcinomatous epithelium revealed lymphocytic infiltration in all of the cases presented. This infiltration varied in degree not only in each case but occasionally in different areas of the same case. It appeared that in this series of cases, there was no correlation between the amount of lymphocytic infiltration and the severity of the lesion.

All of the 15 cases also disclosed an increase in the number of cells of the stratum germinativum and of the epithelium as a whole. In the 6 cases of invasive carcinoma, 3 showed a moderate increase and 3 showed a marked increase. In the noninvasive cases, 6 showed a moderate increase; 2, a marked increase; and 1, a mild increase. The correlation between the severity of the lesion and the increase of cells was not very definite in this group.

Fig. 5. Case 4. This case discloses the cells described as characteristic of early carcinoma in the still intact epithelium, undistinguishable basal layer, and intact basement membrane. No invasion. × 100.

All of the cases also revealed a loss of polarity of the cells. In 4 cases this feature was mild and in 9 cases it was marked. In all of the cases which had invasive carcinoma in other areas of the same cervix, the loss of polarity was marked.

All of the changes previously described were sometimes found in the squamous epithelium which replaced cervical glands as a metaplastic process. Usually the surface epithelium overlying these areas revealed the same changes. Ten cases of metaplasia with changes of early carcinoma in the epithelium of the same cervix were found in the material studied. Three of these cases revealed very little or no carcinomatous changes in the areas of metaplasias. Seven cases (Cases 4, 5, 10, 12, 13, 14, and 15) revealed that the glands with metaplasia were all involved in the changes of early carcinoma. All of these cases showed that the overlying epithelium was also involved in a similar change except in Case 13 where the epithelium was absent due to ulceration. In none of the 7 cases was there an invasion of the basement membrane by the malignant cells in the area of metaplasia. However, 3 of the 7 cases had invasive carcinoma in another area of the same cervix involving the surface squamous epithelium. No attempt was made to relate metaplasia to development of squamous cell carcinoma of the cervix. The finding of metaplasia may have been only coincidental. However, in 8 cases it participated in the early changes of carcinoma in a manner similar to the participation of the surface squamous epithelium.

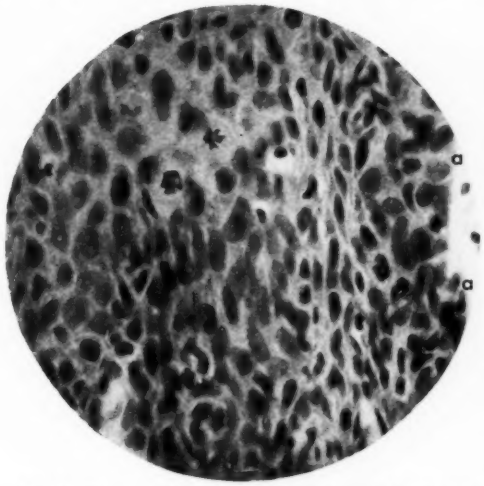


Fig. 6. Case 4. High power photomicrograph of same case as Fig. 5. The undistinguishable basal layer is present at *a* (Right). × 395.

Fig. 7. Case 5. The case discloses metaplasia combined with the morphological changes of carcinoma in the epithelial cells of the metaplastic areas. In the surface epithelium there were also changes of early carcinoma. × 100.

There were 2 cases of leucoplakia existing together with the morphological changes of early carcinoma in the squamous epithelial cells. In 1 case the basement membrane was intact throughout the cervix and in the other the basement membrane was invaded in areas. Case 9 showed the invasive carcinoma together with leucoplakia. In this case the areas of early carcinoma with an intact basement membrane in the same cervix revealed the squamous epithelial cells were characteristic of early carcinoma. Case 6 disclosed leucoplakia together with early carcinoma with an intact basement membrane throughout the entire cervix.

Cases 10 and 15 were studied in which only the changes of early carcinoma were seen in several original microscopic sections of the cervix. However, because of the suspicious character of the lesions, further investigation of these cervices by means of additional sec-

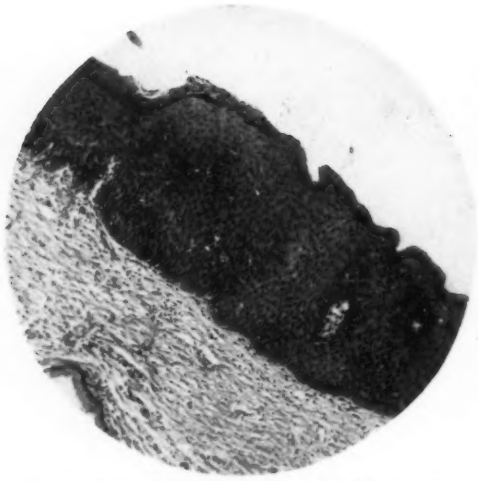


Fig. 8. Case 6. This case reveals leucoplakia combined with the morphological changes of early carcinoma. Hyperkeratosis and parakeratosis can be seen, together with hypertrophy of stratum germinativum. Increased irregularity in size and staining of cells of stratum germinativum, mitotic figures, increase of basal layer cells with indistinguishable basal layer are also seen. × 100.

tions from various areas was made, and invasive carcinoma was discovered. This would not have been suspected by the appearance of the cervix from clinical or gross pathological studies and indicates the value of biopsy in the abnormal cervix. In Case 10 the cervix was removed with the uterus with the clinical diagnosis of chronic cervicitis with erosion. In Case 15 the first biopsy revealed evidence suspicious of early carcinoma and the cervix was subsequently removed for further investigation and study.

COMMENT

A series of 15 cases of early carcinoma of the cervix uteri as reviewed; 9 of these disclosed no invasive carcinoma elsewhere in the cervix and 6 revealed early invasive carcinoma in the same cervix.

The criteria of early noninvasive carcinoma were interpreted as possessing the following characteristics: (1) The squamous epithelial cells had a decreased amount of cytoplasm with deeply stained, oval nuclei. These changes were found in all of the 15 cases. (2) All cells of the epithelium resembled each other closely from the basal to the uppermost layer so that the basal layer was not distinguishable. This change was observed in 12 cases. (3) In all cases, there was an increase in the number of cells of the stratum germinativum. (4) In 14 cases mitotic figures were present. (5) The basement membrane was not penetrated in any of the noninvasive cases. (6) The subepithelial tissue in all cases was infiltrated with lymphocytes. (7) Seven of the cases disclosed a line of demarcation between normal and carcinomatous epithelium. In 3 of these the transition was gradual and in the others, the demarcation was abrupt and distinct. (8) All 15 cases showed a loss of polarity of the cells. (9) The changes of early carcinoma were also found in areas of coexistent metaplasia in 8 cases. Usually the epithelium overlying these areas was involved in the same process. (10) In 2 cases leucoplakia existed in conjunction with the changes of early carcinoma in the surface epithelium. In 1 of these 2 cases invasive carcinoma was disclosed in some areas.

Two cases were seen in which the diagnosis of early noninvasive squamous cell carcinoma of the cervix uteri was made, which upon further study, because of this diagnosis, disclosed early invasive carcinoma. These examples indicate the value of biopsy and also the value of further investigation of the cervix uteri in cases in which early noninvasive carcinoma has been diagnosed.

As a result of this study the earlier work of Rubin, Meyer, Schiller, Broders, and others is confirmed; namely, that cellular changes develop in the surface stratified squamous epithelium of the portio vaginalis of the cervix which are regarded as the early manifestations of malignant transformation. That these changes occur before there is invasion and before there is clinical evidence of carcinoma is also demonstrated. The report also indicates that the epithelial cellular changes are similar in noninvasive and early invasive carcinomas in areas not yet frankly or clinically carcinomatous, and closely resemble the changes found in the epithelial cells of frankly or clinically carcinomatous lesions. This tends to support the thesis that the so called intraepithelial preinvasive changes as described are the earl-

iest signs and the forerunner of carcinoma of the cervix uteri.

SUMMARY

A series of 15 cases of early carcinoma of the cervix uteri is presented. These cases reveal changes in the surface squamous epithelial cells which have been interpreted as the early cellular transformations of malignancy in the preclinical preinvasive stage of carcinoma. The changes stand comparison with previously described early invasive squamous cell carcinomas of the cervix and are similar to the changes which are found in clinical frankly invasive squamous cell carcinomas of the cervix uteri. These changes have been described in detail.

REFERENCES

1. BRODERS, A. C. J. Am. M. Ass. 1932, 99: 1070–1074.
2. MEYER, R. Surg. Gyn. Obst., 1941, 73: 14–20; 129–139.
3. NOVAK, E. Surg. Gyn. Obst., 1937, 64: 977–988.
4. RUBIN, I. C. Am. J. Obst., 1910, 62: 668–676.
5. SCHILLER, W. Surg. Gyn. Obst., 1933, 56: 210–222.

ACUTE INJURIES TO THE NECK INVOLVING THE FOOD AND AIR PASSAGES

MANUEL E. LICHTENSTEIN, M.S., M.D., F.A.C.S., Chicago, Illinois

INJURIES involving the soft tissues in the neck vary in extent and significance from the trivial, superficial, and inconsequential to the most extensive, deep, disabling, life endangering, and fatal. The proximity of important structures concerned with the vital functions confined to a small part of the body may account for the small number of patients with severe or serious injuries since it is likely that many die soon after wounding from exsanguination, strangulation or aspiration of blood into the bronchial tree. Those who survive the immediate injury are threatened with mediastinitis due to leakage of nonsterile secretions into the retropharyngeal space. This complication is often the cause of death in fatal cases.

Injuries to the soft tissues of the neck in civilian practice occur only occasionally. Stab or gunshot wounds, penetration of glass fragments, and surgical accidents with injury to the trachea, pharynx, or other structures account for some, while injuries due to the swallowing of pins, needles, fish bones, tooth picks, and partial plates account for others.

This report concerns a group of patients who sustained injuries to the food and air passages in the neck, admitted to an evacuation hospital during the Italian campaign. Injuries involving the large vessels of the neck have been reported previously (1). The details of management in this series are presented with the hope that similar reports may help to establish the principles of immediate management of injuries to this part of the body.

CASE 1. Pfc. W., aged 42 years, was injured in a mine explosion at 10:00 p.m. October 17, 1944 and was admitted to the hospital on October 18, at 4:00 p.m. He sustained a penetrating wound of the chin near the midline between the hyoid bone and mental process with lodgment of the missile in the body of the 3rd cervical vertebrae. The missile traversed the pharynx leaving entrance and exit wounds which opened into the fascial spaces of the neck. An x-ray examination disclosed air in the retropharyngeal space. At 10:00 p.m. October 18, under nitrous oxide-oxygen-ether anesthesia administered by the endotracheal method, an incision was made along the anterior border of the upper ½ of the left sternomastoid muscle. Fascial spaces of the neck were exposed and the foreign body was removed from the 3rd cervical vertebra. The contaminating secretions of the pharynx were sponged from the wound, and the wound was left open. The posterior wound in the pharynx was exposed but not sutured. Food and water were administered by means of a tube passed through the nose into the stomach from October 18th to 28th. The wound was closed by positioning the head without suture on October 25, and was healed on November 6, at which time he was evacuated to a base hospital for further observation (Fig. 3). Penicillin was given in 25,000 unit doses every 3 hours intramuscularly for 7 days. The entire course was free from complications during the 19 day stay in the hospital.

CASE 2. Sgt. Santos, aged 24 years, was wounded by a sniper's bullet at 3:00 a.m. January 9, 1945 and was admitted to the hospital at 4:15 p.m. of the same day. The missile perforated the upper lip on the left side, entered the mouth, perforated the tongue, traversed the pharynx, and lodged between the 2nd and 3rd cervical vertebrae. In addition he sustained injuries to the buttocks and extremities. An x-ray examination showed air in the soft tissues of the neck down to the mediastinum. At 9:00 p.m., under nitrous oxide-oxygen-ether anesthesia administered through an endotracheal tube, the fascial spaces of the neck were exposed through an incision along the anterior border of the left sternomastoid muscle. The foreign body was removed, and the defect in the posterior wall of the pharynx was demonstrated but not closed. The wound was left open without drains. The wounds of the lip and tongue were cleansed and sutured. Feedings were administered for 8 days by means of a tube passed through the nose. Following this he was fed by mouth without difficulty or complaint. By positioning the head and by proper bandaging, the wound was closed without suture. The patient was evacuated to a base hospital on January 20. Penicillin was given in 25,000 unit doses every 3 hours intramuscularly. The postoperative course was free from complications and no evidence of infection was noted at any time.

CASE 3. Pfc. L. was wounded by shrapnel at 5:30 p.m. March 2, and he arrived at the hospital 5 hours later. He sustained a penetrating wound of the right carotid triangle with lodgment of a foreign body in

From the Michael Reese Unit (16th Evacuation Hospital, AUS.), and The Division of Surgery, Northwestern University Medical School.

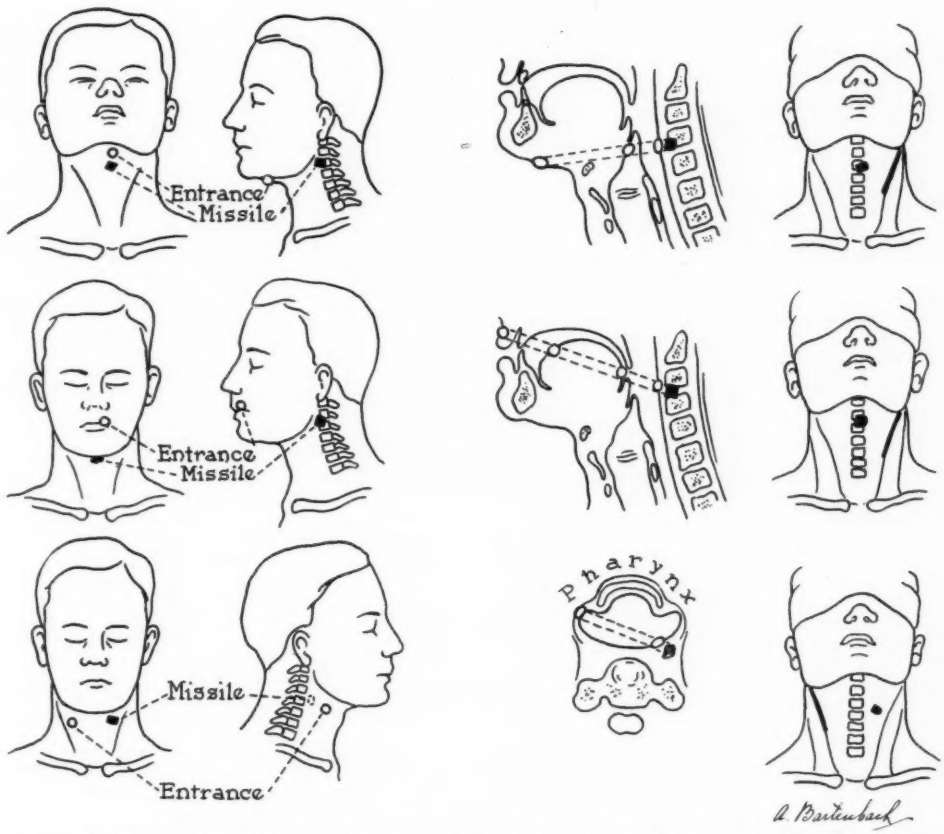


Fig. 1. Sites of entrance and lodgment of foreign bodies, path of gross tissue damage and location of surgical approach, Cases 1, top, 2, middle, and 3, bottom.

the prevertebral space to the left of the midline at the level of the 4th cervical vertebrae. There were two wounds in the pharynx—a right lateral and posterior. Under nitrous oxide-oxygen-ether anesthesia administered through an endotracheal tube the retropharyngeal space was exposed through an incision over the right sternomastoid muscle. The foreign body was removed. No closure of the openings in the pharynx was attempted. He was fed for 8 days through a tube passed through the nose. After this he was able to take liquids by mouth. He was given 25,000 units of penicillin every 3 hours intramuscularly. Patient was evacuated to a base hospital on March 14, with the skin wound not yet healed but ready for closure.

These patients (Cases 1, 2, and 3) sustained injuries to the pharynx with leakage of air and pharyngeal secretions into the exposed spaces in the neck. In the first, the missile lodged in the vertebral body; in the second, the missile lodged in the intervertebral cartilage, while in the third the missile was free in the retropharyngeal space. In all, x-ray examinations disclosed free air in the retropharyngeal space —dissecting down toward the mediastinum (Fig. 2). The danger of infection in the spaces of the neck is well known. Decompression of these spaces by incising the fascial wall for the prevention of infection or treatment of established infection is well known and has been successful in the past. The use of penicillin was routine in each case. The freedom from infection in the presence of pharyngeal secretions in the retropharyngeal space would sug-

Fig. 2. Reproductions of lateral views showing air in the retropharyngeal space in Cases 1, 2, and 3.

gest on the basis of experiences in the past that penicillin was a factor in preserving a clean wound in the postoperative period.

CASE 4. Pvt. H. sustained a large irregular wound on the right side of the neck between the mastoid process and the angle of the jaw from a mortar shell fragment at 5:00 p.m. January 10 and was admitted to the hospital at 10:30 a.m. of the following day. He had considerable difficulty in breathing and swallowing. There was a marked bulge in the posterior pharyngeal wall almost occluding the larynx and the mucous membrane was hemorrhagic and swollen. On x-ray examination a large foreign body was disclosed lying anterior to the 1st and 2nd cervical vertebrae projecting beyond the midline (Fig. 5).

A tracheotomy was done under local anesthesia at 12:00 noon and after stabilization of his general condition ether anesthesia was induced through the tracheotomy tube at 5:00 p.m. Provisional control of blood flow in the right carotid artery was provided through an incision along the anterior border of the right sternomastoid muscle. The retropharyngeal space was exposed and the large foreign body (3 cm. long, 1.5 cm. wide, 1 cm. thick) was withdrawn through the wound of entrance. It was found that no large vessels were injured and the pharynx was not perforated. The wound was cleansed well, damaged tissue was removed and small bleeding vessels were ligated. All wounds were left open. Sulfadiazine in 5 gram doses was given intravenously for 2 days and by mouth for an additional 3 days. The tracheal tube was removed on the 3rd day. Progress was satisfactory and the patient was evacuated to a base hospital on January 18 in good condition.

The large size of the foreign body, the site of penetration and lodgment in the neck, and the small extent of damage found at operation attest to the rôle "chance" plays in the life of the wounded soldier. The retropharyngeal space was contaminated by the foreign body but no evidence of infection was ever disclosed.

Fig. 3. Case 1. Method of wound closure effected without suture.

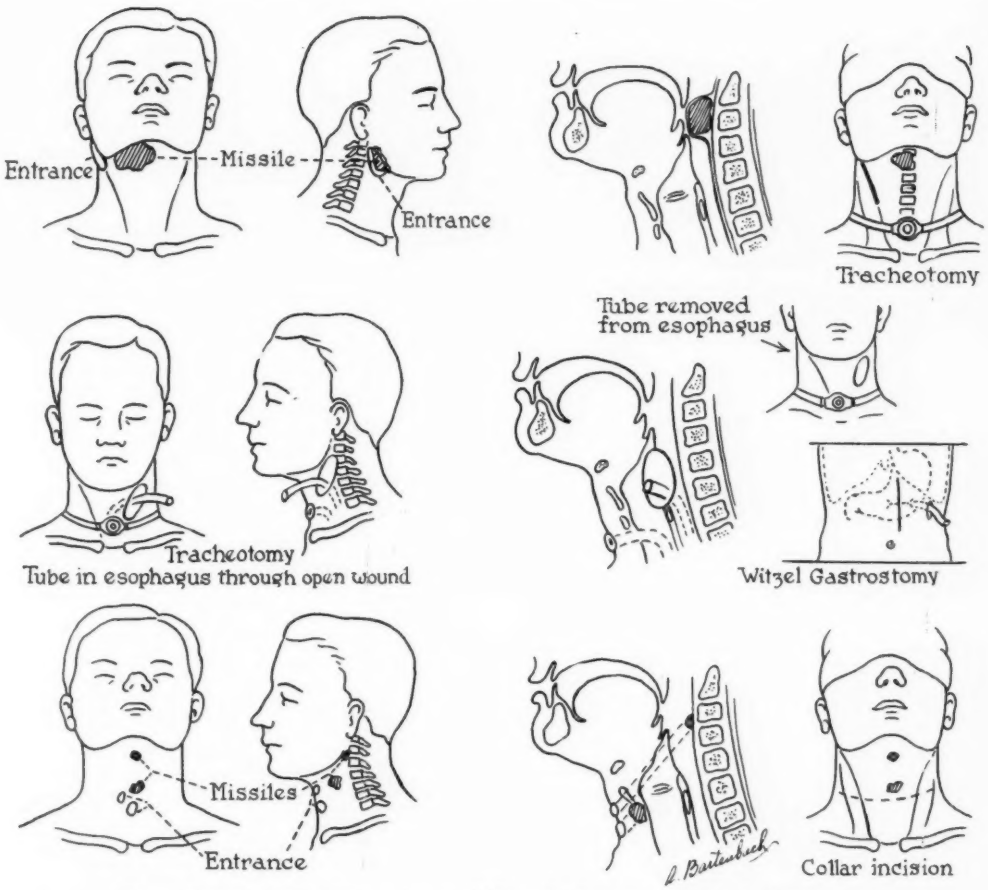


Fig. 4. Sites of injury in Cases 4, top, 5, middle, and 6, bottom, and methods of treatment.

CASE 5. Pvt. R., aged 25 years, sustained a shell fragment wound of the neck on October 26, 1943 at 12:45 p.m. and was admitted to an evacuation hospital on the same day. While here a tracheotomy was done because of laryngeal injury and a catheter was passed into the esophagus through the débrided external wound on the left side of the neck. He was transferred to another hospital on November 5. His general condition was poor. He had repeated hemorrhages from the neck wound and bled profusely from the mouth. Repeated blood tranfusions were given to restore his blood volume. The catheter in the external wound was removed and a tube for feeding was passed through the nose. This decreased the frequency of the hemorrhages, but bleeding was still a daily occurrence. On November 12, a Witzel type gastrostomy was done, under local anesthesia, for feeding and the intranasal tube was removed. He had no further hemorrhages; bleeding ceased from the wound; and, his general condition improved markedly. He was transferred to a base hospital on November 16, 1944 where he continued to improve. He was then evacuated to the Zone of the Interior.

This patient sustained a severe injury in which hemorrhage and infection were the immediate dangers. The cessation of bleeding with removal of the feeding tube passed through the pharynx suggests that pressure and irritation provoked bleeding from granulating surfaces or injured pharyngeal vessels rather than an injury to a large artery or vein.

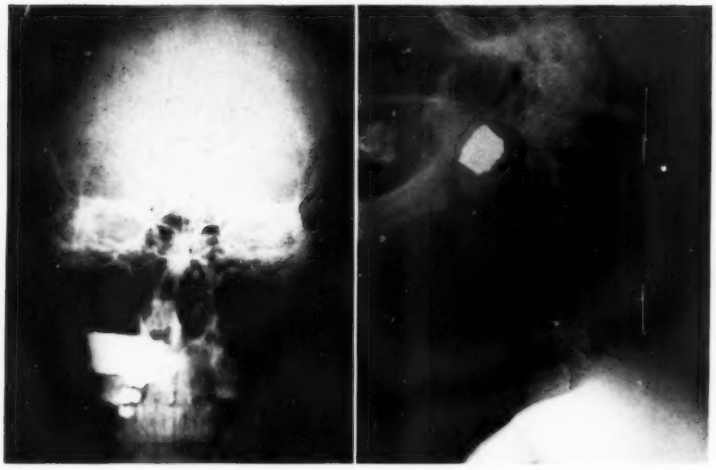


Fig. 5. Case 4. Note size of foreign body especially in its penetration beyond the midline.

The simple gastrostomy, an important measure in this case, provided a means for administering an adequate diet and fluids without disturbing the patient with intravenous or nasal tube feeding. The procedure is valuable and should not be relegated to the position of a "final resort" in a "hopeless" situation.

CASE 6. Pvt. B., aged 21 years, sustained shell fragment wounds of the neck, chest, and left forearm at 9:00 a.m. January 11 and was admitted to the hospital at 11:30 p.m. of the same day. He coughed frequently with bloody expectoration. There were 2 entrance wounds on the anterior aspect of the neck, little swelling of the neck but pain on pressure over the trachea. X-ray examination disclosed 2 foreign bodies in the midline—one anterior to the cartilage between the 2nd and 3rd cervical vertebrae and the other at the level of the 4th cervical vertebra in contact with the larynx.

Under nitrous oxide-oxygen-ether anesthesia, the wounds were exposed through a collar incision. Damaged laryngeal cartilage was removed and the retropharyngeal space was exposed. One large foreign body with cloth attached was removed.

The patient was fed through a tube for 2 days after which he took liquids by mouth. There was no wound drainage. Sulfadiazine was given in 2½ gram doses intravenously twice daily for 5 days.

He was evacuated to a base hospital on January 17 where wound healing continued satisfactorily.

In other case reports in this series and in another series of vascular injuries of the neck, an incision along the anterior border of the sternomastoid muscle was used most frequently. In this case a collar incision served to expose the wound tracts and involved spaces. Incisions are made for a purpose and neither the collar incision nor the oblique incision can be regarded as routine practice. In each case a survey is made of the sites of injury, structures that must be exposed, and the structures that must be available in the wound if one is to prevent needless loss of blood and tissue damage. Collar incisions are preferable but their use is secondary to the requirements of the case. In this instance one small foreign body was not removed but no follow up examination was possible and the effect of this requires further investigation.

CASE 7. Pvt. K., aged 19 years, sustained shell fragment wounds of the neck, right shoulder, left forearm, and right leg some time before noon June 28, 1944 when he was given first aid and sent to a field hospital at 1:05 p.m. Here because of dyspnea and cyanosis a tracheotomy was done and the patient was evacuated to the hospital at 4:15 p.m. of the same day. On examination the neck presented two large defects with extensive loss of tissues. The entrance wound was about 1 inch in diameter to the left of the midline above the clavicle—the exit wound was 3 inches in diameter on the right side of the neck below the chin. All the intervening tissues had been "blown" out. The entire larynx and ⅔ of the cricoid cartilage were absent and the anterior and lateral walls of the pharynx were missing. Below the hyoid bone there was a large cavity leading in-

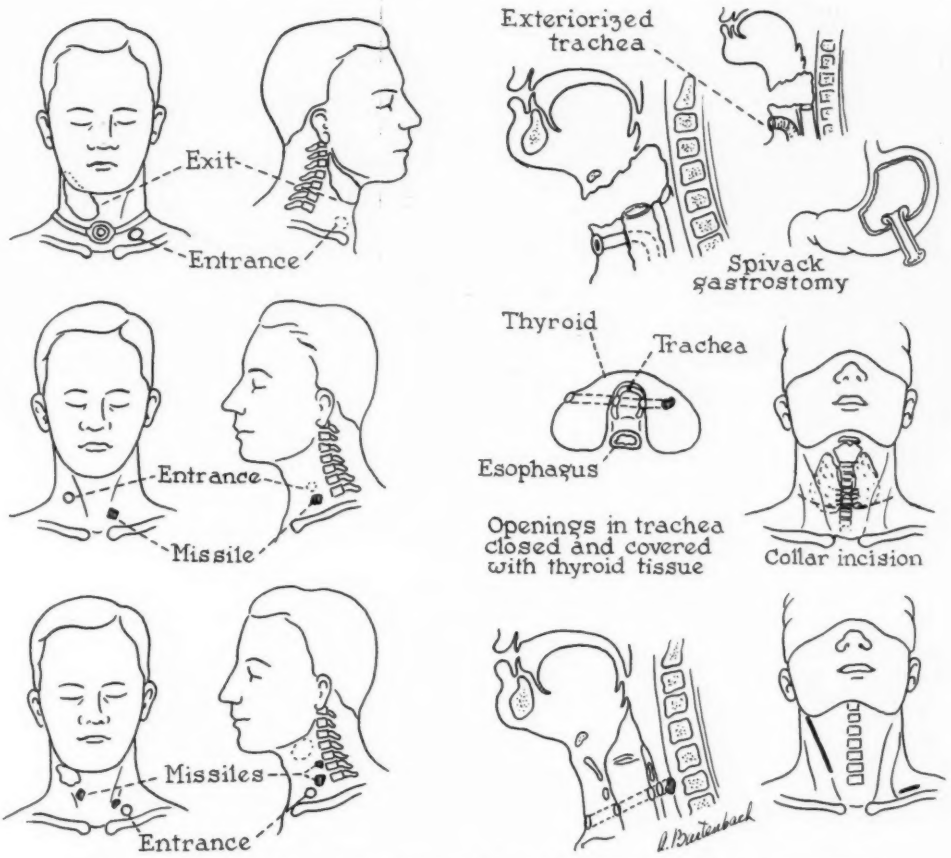
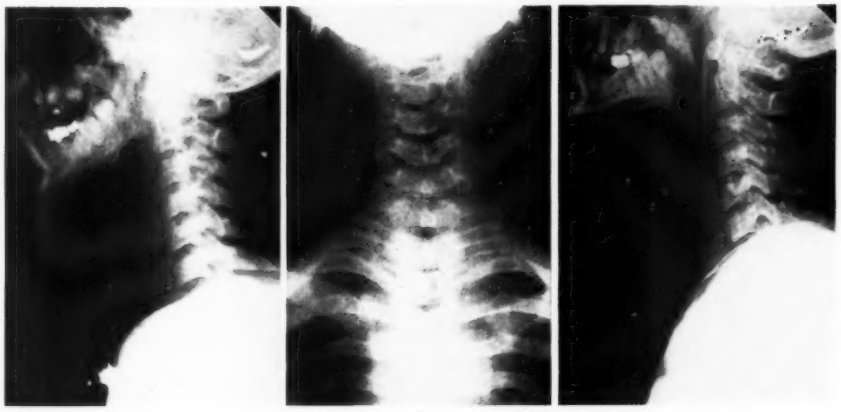


Fig. 6. Location of injuries in Cases 7, top, 8, middle, and 9, bottom and method of management.

feriorly into the trachea and the esophagus. A large portion of the left sternomastoid muscle was missing. The right common carotid artery was exposed in the field. Smaller vessels were thrombosed and the wound was free from hemorrhage. In addition he sustained compound fractures of the left clavicle, right ulna, and right tibia. There was an extensive accumulation of nasopharyngeal secretions which were controlled with atropine and mechanical suction. With oxygen therapy and 1,000 cubic centimeters of whole blood his condition improved. Under ether anesthesia administered through the tracheotomy tube the wounds were cleansed, damaged tissues excised, and splints applied to the extremities. His general condition was not good. He could not tolerate a feeding tube and was maintained on intravenous proteins, salts, dextrose, and vitamins. On July 2 a tubovalvular type gastrostomy was done. He was fed through this and gained considerably in weight and strength. Because of repeated bouts of aspiration pneumonitis, the tracheal orifice was exteriorized. A narrow zone of pharyngeal mucous membrane, 1 centimeter wide, extended from the nasopharynx to the esophagus. By July 20 he was up and about able to feed himself through the new gastric stoma. He was evacuated on July 24 to a base hospital where the neck wound healed.

This patient sustained a severe injury with extensive loss of substance to the air and food passages of the neck. The gastrostomy in this case was of a type which did not require the presence of a catheter for patency. The valvular effect prevented leakage following filling of the stomach. Exteriorization of the trachea prevented aspiration of nasopharyngeal se-



a b c

Fig. 7. Case 7. Loss of larynx, cricoid cartilage, and anterior wall of pharynx following passage of a missile through the neck. a, On admission with tracheotomy tube; b and c following exteriorization of trachea.

Fig. 8. Case 9. Emphysema of soft tissues following tracheal injury.

cretions. A narrow strip of posterior pharyngeal wall suggested the possibility of reconstruction of the pharynx by a plastic procedure. However, the large cutaneous defect precluded such a procedure at this time.

CASE 8. Sgt. F., aged 24 years, sustained a shell fragment wound of the neck at 3:00 p.m. on May 12, 1945 and arrived at a clearing station at 5:00 p.m. where one unit of plasma was administered. He was evacuated and arrived at the hospital at 7:00 p.m. of the same day. He was dyspneic and coughed with a bloody expectoration. The neck was swollen and emphysematous. A small wound was noted to the right of the midline below the level of the cricoid. An x-ray examination disclosed a metallic foreign body to the left of the midline anterior to the 7th cervical vertebra with considerable air in the soft tissues of the neck (Fig. 7). Under nitrous oxide-oxygen-ether anesthesia administered through an endotracheal tube after cocainization of the larynx, a transverse incision was made exposing the tract of the wound. The trachea was perforated. The missile transversed the thyroid gland at the isthmus, passed into and out of the lumen of the trachea, and lodged in the soft tissues to the left of the midline. The damaged thyroid tissue was excised, and bleeding vessels were ligated, the openings in the trachea were trimmed, sutured loosely and covered with ad-

jacent thyroid tissue without tension. The foreign body was removed and the collar incision left open. The patient made satisfactory progress. There was no drainage from the wound and when the patient was evacuated to the base hospital on May 20 the wound was well closed without suture.

This patient illustrated a phenomenon noted in other patients with injuries to the neck. Dyspnea of mild or severe degree is noted frequently especially in vascular injuries but also in any case in which swelling of the neck involving the deep structures develops acutely. It has been found that breathing in the postoperative period is free from difficulty when the fascial spaces are exposed by incision of the tense fascial sheaths.

CASE 9. Sgt. W., aged 25 years, sustained penetrating grenade fragment wounds of the neck early on June 4, 1944, and was admitted to the hospital at 7:00 p.m. of that day. There was a loss of skin resulting in an irregular defect 4 by 2 centimeters in size at the junction between the chin and the neck on the right side and an irregularly shaped wound 1 centimeter in diameter posterior to the left sternomastoid muscle above the clavicle. The neck was swollen with air in the soft tissues. A cough was associated with a bloody expectoration. An x-ray examination disclosed a foreign body at the level of the anterior surface of the 6th cervical vertebra to the right of the midline and another in the left supraclavicular fossa (Fig. 8). The larynx was swollen and hemorrhagic, the air passage reduced about 50 per cent in size.

Under nitrous oxide-oxygen-ether anesthesia administered through an endotracheal tube, the wounds in the neck were freed from damaged tissue and the foreign bodies were removed. An exploration of the large vessels, larynx, and trachea was made through an incision along the anterior border of the right sternomastoid muscle and also a supraclavicular incision on the left side. Aside from some small bleeding vessels, only the larynx sustained a perforating wound. The edges of the entrance and exit were excised and the wounds were closed with adjacent tissues. The surgical wounds were sutured. The endotracheal tube was left in place for 1 hour in the postoperative period. Breathing subsequently was unimpaired and the patient progressed satisfactorily. He was evacuated to the base hospital on June 8 in good condition.

In the patients who sustained acute injuries to the respiratory passages, immediate closure of the perforation was done at the time initial surgery was undertaken. It is noteworthy that dyspnea frequently present on admission to the hospital was no longer present in the immediate postoperative period and did not recur. Exposure of the fascial spaces in the neck appeared to be the factor responsible for this freedom from dyspnea.

SUMMARY

1. Injuries to the air and food passages in the neck are not common in patients admitted to an evacuation hospital.

2. Tracheotomy may be necessary and urgently so when signs of obstruction are noted. However, in many instances of neck wounds with dyspnea—incision into the fascial spaces as part of the initial surgery of the wound was followed by relief from the signs and symptoms of obstruction.

3. Anesthesia may be administered through the tracheotomy tube or through an endotracheal tube. Aspiration of the trachea and bronchi may be accomplished easily. This is an important factor in the avoidance of pulmonary complications. For wounds of small magnitude, local anesthesia is useful.

4. When contamination of the deep neck structures has occurred because of perforation of the oral, pharyngeal or esophageal mucous membrane, incision into the fascial layers with exposure of the retropharyngeal space prevents edema and spread of infection into the mediastinum.

5. The value of gastrostomy in certain wounds of the pharynx and esophagus should be appreciated and the operation done while the patient is in good condition when tube feeding through the nose is not possible.

6. Tracheal wounds when not too extensive tend to close or may be closed by suture of the overlying fascia, muscle, or adjacent thyroid tissue.

7. The skin wounds adjacent to openings in the food and air passages are left open until it is certain the wound is free from gross infection. Closure of the wounds may be done after 5 days by suture or by positioning of the head and purposeful bandaging.

8. Penicillin is used routinely and appears to be a factor in the avoidance of local and spreading infection.

REFERENCES

1. LICHTENSTEIN, MANUEL, E. Surg. Gyn. Obst., 1947, 85: 165-175.

THE TREATMENT OF PANCREATIC PAIN BY SPLANCHNIC NERVE SECTION

GEZA deTAKATS, M.D., F.A.C.S., and LEROY E. WALTER, M.D., Chicago, Illinois

OF the many causes of abdominal pain, the one caused by affections of the pancreas is one of the most severe and most intractable. One can readily distinguish two components. The first is visceral, due to the direct or transmitted stimulation of the celiac ganglion, accompanied by girdle pain around the waistline and radiating fanwise to the lower abdomen. This pain is continuous, but shows intermittent, lancinating exacerbations, not unlike that of a tabetic crisis. Carcinoma of the body of the pancreas, acute pancreatic edema and chronic sclerosing or calcareous pancreatitis, all may exhibit such symptoms.

When the lesion extends to the peritoneum, the somatic sensory fibers of the lower intercostal or upper lumbar nerves or even the branches of the lumbosacral plexus are irritated. This somatic pain shows skin hyperesthesia in the appropriate segments and sensitivity of the spinous processes of the segmental zones. Muscle rigidity may appear.

Paravertebral block of the corresponding segments extending in the case of the pancreas from the sixth to the tenth dorsal level abolishes visceral pain but only so much of the somatic pain which happens to travel through that area. Mandl, in his pioneer monograph on paravertebral injections, gave many examples of relieving colics originating in gastroduodenal, gall-bladder, renal or other visceral lesions. No mention was made, however, of pancreatic pain. One of us (G. deT.) in a monograph on local anesthesia, advocated the use of diagnostic paravertebral injections for the differentiation of upper abdominal pain.

Intractable pain from the gastrointestinal tract or from the biliary passages has been relieved by paravertebral block with alcohol or by splanchnic nerve section, and such instances are on record from the case reports of White and Smithwick who also summarized the previous literature. Craig, in 1934, relieved chronic biliary pain by his infradiaphragmatic splanchnicectomy. The pain of gastroduodenal ulceration has been reported to have been relieved by a number of authors even though the aggravation of the ulcer has been suggested by the creation of a relative vagotonia. In the case of Weeks and associates (4b), a painless duodenal perforation occurred in the sympathectomized patient.

The French literature contains an extensive study on the effect of splanchnicectomy in chronic pancreatitis. Mallet-Guy and his coworkers reported 11 such cases, in which unilateral splanchnic nerve section was done. Of these, all had immediate relief after unilateral (left) splanchnic section, but 1 patient showed a recurrence of pain after 5 months; another had only a short follow-up and could not be reexamined; 9 patients had complete relief lasting as long as 2 to 3 years. These patients had all been subjected to exploratory laparotomy and biliary drainage had been unsuccessful in relieving their symptoms. The left splanchnic nerve was sectioned in 10 of the 11 cases below the diaphragm, often with difficulty because of the inflammatory reaction in the retroperitoneal tissues. In 1 case the right splanchnic nerve was cut.

From the same institution, Marion reported the treatment, with splanchnic anesthesia, of 7 patients with acute pancreatitis thus promptly relieving the pain and postponing immediate laparotomy.

In a recent article written by pupils of Leriche (3) 1 case was reported in which splanchnic resection was undertaken for chronic pancreatitis. One case of this sort was also mentioned by Smithwick in a discussion of Whipple's paper on radical surgery for certain cases of calcareous pancreatitis, but to our knowledge it is yet unpublished.

From the Department of Surgery, University of Illinois College of Medicine and the Research and Educational Hospitals. Paper read at the Chicago Surgical Society May 2, 1947.

We wish to report 2 cases in which unilateral splanchnicectomy was performed for intractable pancreatic pain.

CASE 1. C.H., Hospital No. 108768. A 49 year old white male was admitted to the Research and Educational Hospital on December 10, 1946, with complaints of pain in the epigastrium radiating posteriorly to the back which had been present for 3 months prior to admission. There had been vomiting shortly after meals for the 10 days prior to admission, shortness of breath, and constipation of 3 months' duration. The pain was described as constant and dull aching, starting in the midepigastrium just to the right of the midline and radiating posteriorly to the back in the midline around the level of the lower dorsal vertebrae. There was a weight loss of 15 pounds in 3 months and a marked anorexia. There was no history of clay colored stools or dark urine.

Physical examination revealed a patient of emaciated appearance and chronically ill in appearance. Temperature was 97.0 degrees, pulse, 70; respirations, 25, and weight was 138 pounds. The heart was normal. There were a few expiratory wheezing râles in the right upper lobe. The abdomen was flat but there was a sense of fulness in the epigastrium, although no definite mass was palpated. The upper abdomen in the midepigastrium was moderately tender as were the left hypochondrial and left lumbar areas. Rectal examination was negative. The red blood cell count was 3,730,000, white blood count 9,800. Serum amylase was 146 on December 21, 1946, 612 on December 30, 1946, and 61 on January 11, 1947. Total proteins were 7.5 per cent with a serum albumin of 5.5 per cent and a serum globulin of 2.0 per cent. Fasting glucose was 143 milligrams, nonprotein nitrogen, 38, and chlorides 511 milligrams per 100 cubic centimeters. An upper gastrointestinal roentgenogram and barium enema were reported as normal. Roentgenogram of the chest revealed a circular density to the left upper lobe considered to be a metastatic lesion. Roentgenogram of the dorsal spine was negative. After adequate preparation for surgery, which consisted in part of multiple blood transfusions, the patient was operated upon on January 2, 1947 by Dr. Warren H. Cole. When the peritoneum was opened a large tumor mass, occupying the posterior portion of the pancreas and extending upward to the liver edge was seen. The tumor was estimated to measure 3 by 3 by 5 inches. There were no metastases to the liver, although the superior extension of the tumor consisted chiefly of metastatic nodes. In spite of the probable metastasis to the lung, resection appeared indicated, in view of the patient's extreme pain. However, closer inspection of the tumor revealed a superior portion of the mass with its metastatic nodes to completely surround the celiac axis. The hepatic artery could be felt coming out of the center of the mass. This one point, in addition to the complete incurability, caused the decision against resection to be made, so the abdomen was closed.

In the postoperative period, this patient's pain continued and required large doses of narcotics and sedation for effective relief. However, even heavy doses of narcotics failed to give him adequate relief. For these reasons consideration was given to the possibility of splanchnic nerve block, and perhaps resection of the nerve if indicated by a favorable response to the block. On January 10, 1947 a right paravertebral sympathetic block was done from sixth to the tenth dorsal, injecting 10 cubic centimeters of 1 per cent novocain at each level. Twenty minutes after the block, the patient stated that the epigastric pain had completely disappeared. For 12 hours after the block there was no return of pain. The patient had not received sedation or narcotics for 8 hours preceding the block.

On January 14, 1947, under intratracheal anesthesia, Dr. Geza deTakats performed a resection of the right splanchnic nerve from the level of the diaphragm to seventh dorsal. The sympathetic chain was also excised from above ninth dorsal to below the twelfth dorsal. A small tear was made in the pleura during this dissection, which was closed with interrupted cotton sutures.

Convalescence from this operation was uneventful and there was prompt relief from the epigastric pain. He was discharged from the hospital on January 23, 1947, 9 days after the splanchnicectomy. At the time of discharge he was eating well and had gained several pounds in weight. The relief of pain, however, lasted for only a period of 3 weeks postoperatively. Deep roentgen-ray therapy to the pancreas was begun on January 31, 1947, and shortly after this the epigastric pain returned. The pain became progressively more severe, and again it was necessary to administer narcotics for effective relief. The patient refused rehospitalization and became progressively worse. Death occurred on March 4, 1947. Permission for an autopsy was not obtained.

CASE 2. J.A.W., Hospital No. 109477. A 22 year old white, unmarried female was admitted to the Research and Educational Hospital on December 15, 1946, with complaints of extreme, constant aching pain in the epigastrium radiating to the left flank. She had been well until December, 1945, when she first had noted a dull intermittent pain in the left lumbar area radiating in a radicular fashion to the left hypochondrium. These attacks of pain would occur several times daily and occasionally be associated with vomiting and extreme weakness. She had been hospitalized at another hospital in January, 1946, and we were informed that a left heminephrectomy of the lower pole had been performed at this time, because of a diagnosis of carbuncle of the kidney. The patient remained in the hospital for a period of 5 weeks. The pain persisted after surgery, and 2 weeks following her discharge from the hospital she was readmitted, remaining in the hospital until August, 1946. During this period of hospitalization she had had daily chills with temperature elevations to 104 degrees. During the second hospital stay, she noted a swelling in the epigastrium; there

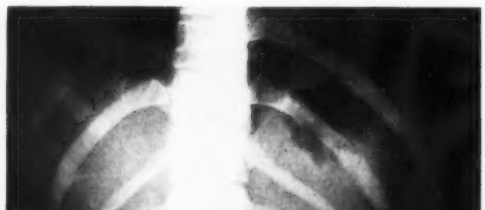


Fig. 1. Film of the abdomen showing a number of calcareous deposits to the left of the spinal column at the level of the first and second lumbar vertebrae. Case 2. Left splanchnic nerve section and lower dorsal sympathectomy completely relieved the patient's intractable pain.

were intermittent episodes of vomiting, a progressive weakness and weight loss, and a relatively persistent pain in the epigastrium and left lumbar region. After a month of hospitalization, the patient was again discharged. Symptoms persisted, and in March the patient went on a alcoholic bout because of pain. Severe diarrhea developed after 1 week of drinking and this caused the patient to terminate her alcoholism. She was hospitalized for the third time and a gastrointestinal x-ray series at this time revealed a large mass present posterior to the stomach and displacing this organ anteriorly. This was interpreted as a large pancreatic cyst. The patient was reoperated upon through the old nephrectomy incision, but there were no reported abnormal findings. One week after the operation a roentgenographic study of the gastrointestinal tract revealed a dramatic reduction in size of the cystic mass. After healing of the lumbar incision, the patient was discharged from the hospital, and stated that she felt somewhat improved, although periodic attacks of pain in the epigastrium and left flank continued to occur. For the 24 hours prior to admission to the Research and Educational Hospital the pain had become severe, and there had been a voluntary dietary restriction, but no vomiting.

On her first admission to this hospital the patient was acutely ill. The temperature was 102 degrees F., respirations 24, and blood pressure 110/60 millimeters of mercury. There was marked dehydration, emaciation, and weakness. The heart and lungs were normal. Diaphragmatic excursions were normal. There was a marked distention of the upper abdomen, especially in the epigastrium, and this portion of the abdomen was rigid. There was also some rigidity of the lower abdomen, but only to a slight degree. The entire upper abdomen was acutely tender. The bowel sounds were active, but not increased. The liver and spleen were not palpable. There was moderate tenderness in the left flank posteriorly. There was no demonstrable fluid wave. Pelvic and rectal examinations were negative. The red blood cell count was 3,800,000 and the white cells were 28,000. The serum amylase was 42 units. On succeeding days the amylase levels were as follows: December 16, 1946, 23; December 21, 38; December 23, 138; December 27, 111; January 4, 1947, 69; January 8, 40; January 11, 43; January 14, 50. The remainder of the blood chemistry on the day of admission was: total protein 6.9 per cent with 4.4 per cent serum albumin, and 2.5 per cent serum globulin. Nonprotein nitrogen was 35 milligrams; glucose was 68 milligrams per 100 cubic centimeters of blood.

A flat plate of the abdomen revealed no free air beneath the diaphragm. There were irregular multiple calcareous densities to the left of the first lumbar vertebra, interpreted as pancreatic calculi (Fig. 1). An intravenous pyelogram revealed no abnormalities.

A Levine tube was inserted into the stomach and continuous Wangensteen suction was instituted. Intravenous fluids were administered. Penicillin 50,000 units every 3 hours was begun. Under this conservative treatment, there was some slight diminution of the pain during the first 24 hours, but the tenderness and epigastric distention persisted. The white blood count was 28,000 the day of admission and then gradually dropped until the fifth day, when it was 14,300. On the third day there was some lessening of the abdominal distention, and considerably less tenderness. A diagnosis of pancreatic lithiasis and pancreatitis with possible pancreatic cyst was made, and following several blood transfusions and further hydration of the patient, an exploratory laparotomy was performed by Dr. Warren H. Cole on December 31, 1946. When the peritoneal cavity was opened, a large mass was found pushing the stomach anteriorly in the midline. The gall bladder was normal. The mass consisted of the pancreas, enlarged to three or four times its normal size, nodular and very firm. The fact that it displaced the stomach forward had resulted in an erroneous preoperative impression that it was a cyst. The entire pancreas was involved in the process, although the tail was not quite so large. Further exploration of the abdomen was unrevealing, and the wound was closed in layers without drainage. The postoperative

course was uneventful. The pain, however, continued and there was severe anorexia with irregular episodes of vomiting, which usually occurred after the intake of even small quantities of food. Parenteral fluid therapy was necessary to maintain the patient's nutritional status at all. Parenteral high vitamin therapy and penicillin were continued, and in addition a course of streptomycin (1 gram per day) was given for a 10 day period. Considerable sedation was necessary to control pain at all times. There was some slight improvement on the fourteenth day after surgery and, at the patient's request, she was discharged from the hospital with instructions to return to the out-patient department in 1 week for observation. Readmission to the hospital occurred on January 20, 1947. The patient stated that, since leaving the hospital, she had had almost continuous pain, nausea, vomiting and weight loss, so that on admission she weighed only 78 pounds. Her problem remained the same—continuous narcotic administration was necessary to control pain, amounting to 3 grains of pantopon a day.

Consideration of splanchnic nerve block or resection was suggested to attempt to relieve this pain and accordingly on January 30, 1947 a dorsal sympathetic block was performed. Ten cubic centimeters of 1 per cent novocain were injected paravertebrally on the left side in each of the segments from the sixth to the tenth dorsal. The block was done in the afternoon, and in the morning preceding the block no sedation or narcotics had been administered. Within 10 minutes after the paravertebral block, the patient reported that there was complete relief of pain, and for the first time in many weeks the patient was comfortable. She slept that night without sedation and felt rested. Because of this result, resection of the left splanchnic nerve was deemed advisable. On February 4, 1947 one of us (G. deT.) performed a left splanchnic nerve resection, including removal of the dorsal sympathetic chain between ninth and twelfth dorsals. This operation was performed under intratracheal anesthesia. The eleventh rib was resected. Reflection of the pleura revealed considerable inflammatory reaction in the posterior mediastinum. The patient tolerated the surgery very well and her postoperative course was uneventful. There was complete relief of the pain in the epigastrium. Abdominal distention disappeared. There was moderate pain over the thoracotomy incision for several days, but no sedation was required after the second day. The patient was ambulatory on the second day, began to eat a general diet, and on discharge from the hospital on February 12, 1947 she weighed 82½ pounds. The patient has remained symptom free up to the most recent follow-up visit on March 20, 1947, and has gained weight steadily. She weighed 107 pounds 2½ months after splanchnic section, a gain of 29 pounds.[1]

Pain relief in the first case was quite temporary. Because of the extensive spread of carcinoma in the peritoneal and retroperitoneal tissues, this was to be expected. However, we were amazed to see the dramatic relief from pain and if confronted with a similar situation, one might prefer an alcohol injection to the lower dorsal segments. The return of pain was not due to the presence of the opposite splanchnic nerve, since it appeared on the right (operated) side.

In the second case the result so far (6 months at this writing) has been lasting. What struck us most was the sudden disappearance of the epigastric distention and one might speculate whether or not this is a direct effect on pancreatic edema and distention or an interruption of reflex pylorospasm. In this connection one must point to the fact that both cardiospasm and pylorospasm produced experimentally by vagal section can be abolished by sympathectomy (5) and that pylorospasm in acute biliary and pancreatic episodes is a frequently recognized clinical entity.

The preoperative diagnostic injections of procaine to appropriate segments is advisable here as before any other form of sympathectomy. It is probable that bilateral splanchnic sections may become necessary if the pain should shift to the side not operated upon. However, the operation may have a direct effect on the inflammatory process and on the vascularity of the gland, thus supplying a direct therapeutic effect (9).

Since the splanchnic nerves are the sensory nerves of the upper abdominal viscera, the question of visceral pain following splanchnic section for hypertension naturally arises (4). Of 250 patients who have undergone splanchnic section done on our service, only a few observations have been made which are germane to this subject. One such patient has been closely studied at our hospital and hence her history is given in detail.

CASE 3. L.S., Hospital No. 106791. A 38 year old married woman had a bilateral splanchnic nerve section done on April 30, 1946 and on May 21, 1946 for a progressive essential hypertension of 13 years' duration, starting with a pregnancy in 1932. Her average preoperative blood pressure was 213/110 millimeters of mercury, and the preoperative workup indicated that she belonged to a group 1 hypertension with little organic damage. She left the hospital with a blood pressure varying from 150 to 126 systolic and 100 to 96 diastolic millimeters of mercury.

[1]Relief of pain persists on re-examination 6 months after operation.

She was readmitted to the hospital 2 months later with itching of the skin, jaundice, dark urine, and a mass in the right upper quadrant of 8 weeks' duration. Eight weeks and 6 weeks before admission she had had episodes of nausea and vomiting following heavy meals. After these attacks, jaundice and a lump in the abdomen appeared. There was no pain at any time, but the nausea persisted. On entrance, the patient's blood pressure was 125/95 millimeters of mercury. She was manifestly icteric and the liver was palpable four fingers below the costal margin. Over the edge of the liver, a tense, tender gall bladder was palpable. The lesion was so painless that prior to admission a diagnosis of homologous serum jaundice was made, since she had received two blood transfusions during each of the splanchnic nerve sections. Of the laboratory findings, the urobilinogen and cephalin flocculation tests were negative, blood bilirubin was 15 units, icterus index was 66, and amylase 116 units.

On August 19, 1946, with a preoperative diagnosis of obstructive jaundice, Dr. Warren H. Cole found a greatly thickened gall bladder containing stones. There were numerous adhesions between the gall bladder, duodenum, and colon. After they were separated, a greatly thickened common duct was opened and at least twenty small stones and one large stone about 2.5 centimeters in diameter were removed. The large stone was found to be impacted in a cystic dilatation of the common duct and was wedged in so as to block the duct. The gall bladder was removed and a T-tube was placed in the common duct. Convalescence was uneventful. The patient was discharged on the 15th postoperative day and the T-tube was removed in 5 weeks.

The percentage of painless jaundice in impacted common duct stones and with a distended gall bladder is not too large, but still common enough not to allow a definite statement that the absence of colic here was due to splanchnic section. More important, however, is the fact elicited after careful questioning that this patient has had upper abdominal distress prior to splanchnic section for 11 years, with occasional bouts of severe pain prior to splanchnic section but never after. Since visceral afferent fibers of the upper abdomen are carried in the splanchnic nerves, the question of eliminating danger signals of threatening perforation may be raised. It must be emphasized that peritoneal irritation is mediated by somatic fibers and that sensation of nausea is known to be mediated through the vagus nerves.

SUMMARY

Two case reports are presented in which unilateral splanchnic nerve section with lower dorsal sympathectomy was done for intractable pain due to pancreatic disease. In the first case the patient was in a terminal phase of an inoperable carcinoma of the body of the pancreas and relief was of short duration. In the second case, that of a chronic recurrent calcareous pancreatitis with exacerbations, the operation resulted in sudden relief now lasting over 3 months in a patient whose pain could not be controlled with heavy doses of narcotics taken over a period of 15 months.

A third case was presented, in which a bilateral splanchnic nerve section undertaken for the relief of hypertension was followed by a painless obstructive jaundice for which an impacted common duct stone was responsible.

The value of paravertebral block, followed if necessary by splanchnicectomy, is emphasized in intractable painful upper abdominal pain of visceral origin. This method has not received the attention it deserves.

Since this article was submitted for publication 2 other cases were studied: one patient had a chronic pancreatitis and the second persistent pain following cholecystectomy. Interruption of sympathetic pathways resulted in relief from intractable pain which now lasts for 2 and 3 months, respectively. In the case of Rienhoff (*J. Am. M. Ass.*, 1947, 134: 20) both splanchnics and both vagi were cut for the relief of pancreatic pain, but in our experience unilateral splanchnicectomy and ganglionectomy suffice.

REFERENCES

1. Craig, W. H. K. West. J. Surg., 1934, 42: 146.
2. deTakats, G. Local Anesthesia. Philadelphia and London: W. B. Saunders Co., 1928.
3. Fontaine, R., Forster, E., and Stefanine, L. Lyon chir., 1946, 41: 279.
4. Froehlich, F., Stephan, F., and Froehlich, C. Presse méd., 1942, 50: 665. (b) Weeks, C., Ryan, B. U., and Van Hoy, J. M. J. Am. M. Ass., 1946, 132: 988. (c) Blegen, H. M., and Kintner, A. R. J. Am. M. Ass., 1947, 133: 1207.
5. Knight, G. C. Brit. J. Surg., 1934, 22: 155.
6. Mandl, F. Die paravertebrale Injektion. Vienna: Julius Springer, 1926.
7. Mallet-Guy, P., Jeanjean, R., and Serveltax, P. Lyon chir., 1945, 40: 293.
8. Marion, P. Lyon chir., 1945, 40: 315.
9. Popper, H. Zbl. Chir., 1933, 60: 2050.
10. Smithwick, R. H. Discussion of paper of Whipple, A. O. Ann. Surg., 1946, 124: 1006.
11. White, J. C., and Smithwick, R. H. The Autonomic Nervous System. 2d ed., pp. 365–371. New York: The Macmillan Co., 1941.

SURGICAL TREATMENT OF IRREDUCIBLE INTUSSUSCEPTION IN INFANTS

J. PEYTON BARNES, M.D., F.A.C.S., Houston, Texas

THE treatment of an intussusception found to be irreducible at operation is the subject of this discussion. The etiology, diagnosis, preoperative and postoperative treatment will not be considered except details which are directly related to the operation.

The incision used is a transverse one, slightly below the umbilicus medially and just above the anterior superior spine laterally. One is usually able to retract the right rectus medially enough for adequate exposure, but its section does no harm. The peritoneum is also cut transversely. In practically all cases the right lower quadrant is the site of the major work, and this incision gives very good exposure of this area.

When it is determined that the intussusception is irreducible, the following steps are carried out:

1. The intussusceptum is sutured to the intussuscipiens, by means of mattress sutures of No. 0 chromic catgut. This step is described in the Jessett operation (Fig. 1).

2. The peritoneum is closed, except for a small opening about 3 or 4 centimeters long (Fig. 2).

3. With a continuous suture, the edges of this peritoneal opening are attached to the serous surface of the intussuscipiens (usually the colon) at a point about 2 inches distal to the placement of the original mattress suture line uniting intussuscipiens and intussusceptum (Fig. 2). As shown, one can place this continuous suture so that the longitudinal band on the colon may be used in the next step. After this third step is completed, the operation then becomes strictly extraperitoneal; thus the danger of peritonitis is avoided.

4. The wall of the intussuscipiens is now opened, and the intussusceptum is pulled out and as it is pulled out toward its origin the initial mattress suture line will be felt between thumb and index finger (Fig. 3).

5. When the mattress suture knots are felt, the double-barrelled wall of the intussusceptum is cut through one-half inch distal to the mattress suture line until both edges are clearly defined, and a guy suture is placed through both walls (Fig. 4).

6. A continuous suture, running or lock, is started through both these edges, being used to maintain hemostasis as the mesenteric vessels are reached and the cutting across of the intussusceptum is continued (Fig. 4, insert). When the intussusceptum is completely severed and removed, the continuous suture is completed and a second guy suture is placed opposite the first. The end-to-end anastomosis has now been completed, all gangrenous tissue has been removed, and the entire resection has been carried out completely extraperitoneal. The illustration (Fig. 5) shows the details.

7. A small sized catheter, about No. 12 or 14 F, which will fit very loosely in the anastomotic opening is passed at least 6 or 8 inches up in the proximal ileum (Fig. 6). The two guy sutures are very helpful in this maneuver. Both guy sutures are removed and the anastomosis is allowed to resume its original position. The final result of this step is shown in Figure 6 insert.

8. The incision in the intussuscipiens wall is closed rather loosely, and the abdominal incision up to the catheter is also closed loosely about it. A silk stitch anchors the catheter to the skin edges so that it cannot be pulled out. This is important (Fig. 7).

Postoperatively these babies must be immobilized for about 72 hours. The catheter is attached to a continuous suction device as soon as the baby is back in bed, and this suction will promptly empty the distended loops of ileum of gas and liquid matter, thus allowing peristalsis to be resumed. Since the catheter goes well up in the ileum it serves exactly as an enterostomy, and being much smaller in diameter than the anastomotic ring it does

Fig. 1. Uniting intussusceptum to intussuscipiens with parallel mattress sutures.

not plug this opening as a tightly fitting tube would. Therefore, it serves a double purpose: by removing the gas and liquid portions it relieves and prevents distention; it also allows the solid and semisolid matter to pass around

Fig. 3. The intussusception is pulled out until the mattress suture line is felt between thumb and index finger. The intussusceptum will be sectioned one-half inch distal to this point.

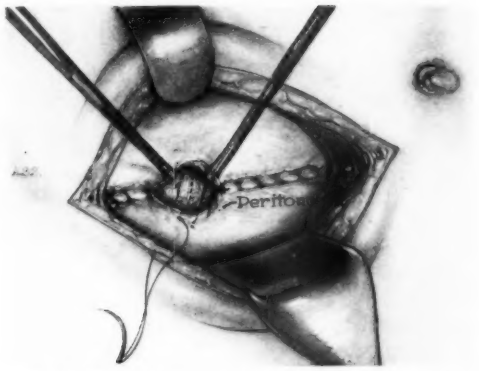


Fig. 2. The peritoneum has been closed with the exception of a small opening. The peritoneal edges are being sutured to wall of intussuscipiens. Dotted line marks site of incision into intussuscipiens.

it and to reach the colon. This promotes recovery of normal bowel action.

CASE REPORT

On December 4, 1946, Baby F, white, male, aged 13 months, was admitted to St. Joseph's Infirmary to the service of Dr. Byron P. York. The obstruction had been present about 36 hours, and abdominal examination showed a lumpy mass extending from the cecal area all the way up the right side and over across the epigastric area to just a little to the left of the midline. Dr. York made a diagnosis of intussusception,

Fig. 4. First guy suture placed through walls of intussuscipiens and intussusceptum. Insert, Intussusceptum cut half way through, running suture being placed.

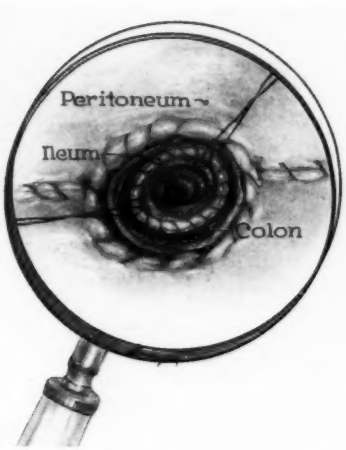


Fig. 5. Close-up view after intussusceptum has been removed. Placement of small sized catheter next.

and operation confirmed it. The ileum had run into itself at a point 2 inches proximal to the ileocecal junction, and passed through the ileocecal valve up the ascending colon and into the transverse colon. The situation as shown in Figure 1 was present. The operative procedure was performed as illustrated, and 18 centimeters of gangrenous ileum were removed. The child made a rapid recovery, leaving the hospital on the sixth postoperative day. He was having normal bowel actions per rectum by the third day. There was very little fecal drainage from the colostomy, which healed rapidly.

It is of historical interest that in 1905 K. Israel reported 2 cases in which, finding an irreducible intussusception, he sutured the colon to the peritoneum about as described here, opened the colon, resected the intussusceptum and sutured the double edges together to effect an end-to-end anastomosis. These cases were successful and demonstrated clearly the value of the extraperitoneal resection, but apparently no attention was paid to his work later. He did not suture the intussuscipiens to the intussusceptum as shown in Figure 1. This suturing together of the intussusceptum and intussuscipiens was described by Jessett, who also opened the intussuscipiens and resected the intussusceptum about as shown here. Jessett did not do an extraperitoneal operation, and apparently closed the opening in the intussuscipiens. Both of these two procedures represent very worth while contributions but the procedure described here adds certain safety factors not present in either one.

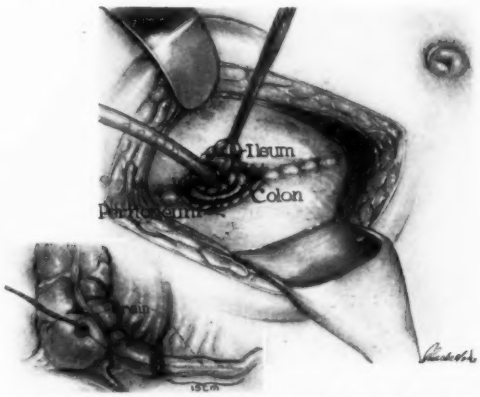


Fig. 6. Loosely fitting catheter being passed well up into proximal ileum. Insert, Anastomosis allowed to slip back to original position, with catheter in ileum.

This procedure may not be applicable in all cases of irreducible intussusception, but where it can be used it has certain advantages of great value.

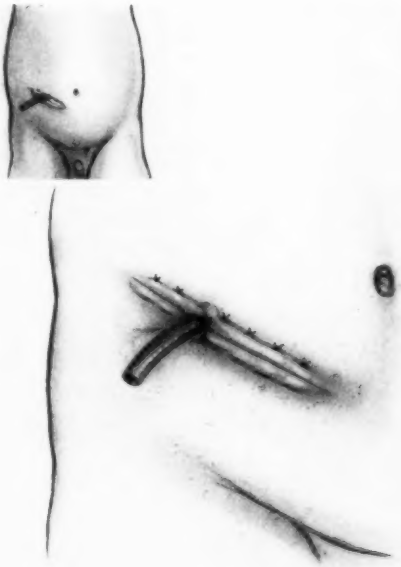


Fig. 7. Abdominal wound closed (more loosely than shown) catheter attached to skin by through-and-through silk suture.

1. It is strictly extraperitoneal after the diagnosis is ascertained, and avoids the danger of peritonitis.

2. No tissue is removed that has not already been destroyed by Nature. Thus no additional shock from resection is added.

3. By means of the catheter passed up into the ileum it provides an enterostomy proximal to the anastomosis.

4. The colostomy provides an additional safety valve of great value. The method employed to provide these two safety valves does not interfere with normal bowel function, but actually promotes it in every way.

5. By not removing any normal undamaged tissue, there is no great loss of body fluids.

6. The operation is easily performed in a short time by an average operator. Since it can be quickly carried out, and also since so little of it is actually intra-abdominal, there is a minimum of shock present, and this is a vital consideration.

SUMMARY

A simple, rapid, mostly extraperitoneal method for the surgical treatment of irreducible intussusception in infants is described.

REFERENCES

1. ISRAEL, K. Med. Record, 1905, 67: 5–20.
2. JESSETT. Described in Brickham's Operative Surgery, vol. IV. Philadelphia: W. B. Saunders & Co., 1924.

THE RELATION OF PROTEIN DEFICIENCY TO EXPERIMENTAL WOUND HEALING

MATHEW W. KOBAK, M.D., EARL P. BENDITT, M.D., ROBERT W. WISSLER, Ph. D., and C. HAROLD STEFFEE, M.S., Chicago, Illinois

DURING the past three decades the importance of protein metabolism in healing processes has been particularly emphasized (4, 5, 9). However, the manner in which lack of protein affects healing is still a matter of controversy. The present investigations were undertaken, therefore, to study further the rôle of protein deficiency in wound healing.

METHODS AND MATERIALS

In order to estimate the results a tensile strength apparatus was developed (Fig. 1). By means of slow release of air from a reservoir bottle into an intra-abdominally placed condom it was possible to measure with a manometer the amount of pressure necessary to disrupt wounds of the abdominal wall of rats. This measurement was recorded automatically with a kymograph. After the point of separation had been determined, the pressure necessary to expand the condom through the previously disrupted incision was also established. The latter figure was considered the base line and represented the pressure dissipated in expansion of the balloon against the enclosing tissues of the peritoneal cavity and through the wound itself. By subtracting the point of separation from the base line an objective estimate of the tensile strength of the wound could be obtained.

Such a system is essentially a variant of that previously reported by Harvey and Howes. However, the present method tests the maximum strength of the wound, whereas in previous devices utilizing air injection the weakest part of the wound allowed escape of the air first. Furthermore, the method of elevating intraperitoneal pressure closely simulates various clinical causes of wound disruption, such as sudden diaphragmatic excursion and ileus with distention.

Young adult male albino rats weighing initially from 180 to 220 grams were used. These were divided into 2 groups, one of which was maintained on a low protein ration containing 1.9 per cent protein (N × 6.25), and the other on a control ration containing 21.1 per cent protein (10). These diets were isocaloric and contained an adequate quantity of vitamins, minerals, and fat. Food was offered in weighed quantities daily. The protein depletion period was 3 months.

Ascorbic acid was not included in the diet because it has been found that the rat can synthesize its own complement of this vitamin. However, the ascorbic acid concentration was determined in the plasma of both depleted and control animals. The levels in both groups of animals were found to exceed 1.4 milligrams per cent.

Postoperatively the rats were maintained in individual cages and were offered 20 grams of the respective diets daily. Food consumption was measured postoperatively in 2 groups of 5 animals each for the purpose of ascertaining the caloric intake in the depleted and control animals. This was done because it has been demonstrated (2) that energy intake is a factor which conditions the utilization of protein. It was found that the normal control animals eating practically all of the diet offered had caloric intakes between 1,150 and 1,250 calories per square meter of body surface per day. The smaller protein depleted animals which were eating slightly less of the low protein isocaloric ration had intakes between 1,350 and 1,850 calories per square meter per day.

Following the period of protein depletion, the animals were fasted for approximately 8 hours, weighed, and anesthetized by the in-

From the Department of Pathology, The University of Chicago School of Medicine.

This work has been aided by the National Livestock and Meat Board and the Douglas Smith Foundation for Medical Research of the University of Chicago.

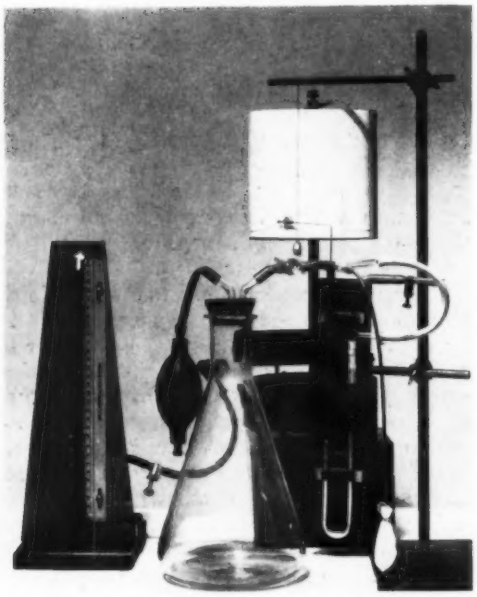


Fig. 1. Apparatus utilized to determine and record the tensile strength of abdominal wall wounds.

TABLE I.—THE INFLUENCE OF PROTEIN DEPLETION ON THE TENSILE STRENGTH OF WOUNDS

Days post-operative	No. of rats	Mean initial weight (gm.)	Mean weight at death (gm.)	Mean weight gain or loss	No. serum proteins	Mean serum proteins	Mean tensile strength of wound—mm. mercury	Standard error, mean tensile strength
Low protein diet								
1	8	214	138	−35	0	4.0	51.0	± 4.09
2	7	212	140	−34	1	3.8	56.8	± 3.92
3	8	218	145	−33	8	4.6	63.4	± 3.51
4	5	211	141	−33	5	4.2	63.4	± 2.38
5	8	212	138	−35	8	4.4	61.5	± 3.91
6	7	211	125	−40	0	—	78.1	± 4.78
7	5	208	140	−32	4	4.8	102.6	± 8.07
9	5	205	120	−38	1	3.4	174.0	± 13.46
Control diet								
1	5	229	293	+28	5	6.6	50.0	± 3.39
2	5	223	291	+17	5	6.1	60.8	± 2.70
3	5	215	314	+40	5	6.2	80.2	± 2.08
5	4	219	297	+35	4	6.2	110.2	± 7.39
7	5	213	313	+47	5	6.5	173.0	± 12.62

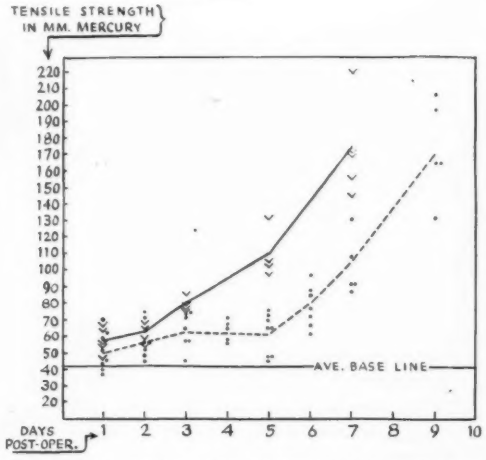


Fig. 2. Comparison of tensile strength of wounds of the abdominal wall in protein depleted and normal control rats. Control diet ———; low protein diet – – – –.

traperitoneal administration of nembutal in doses of 0.07 cubic centimeter per 100 grams of body weight. The wound was then produced by an upper abdominal, left paramedian incision of approximately 2.5 centimeters in length. Three stainless steel wire sutures were used in a through-and-through repair. On selected postoperative days the animals were again fasted, weighed, and anesthetized with ether, and blood was withdrawn for serum protein determination (1, 3). The rats were then sacrificed in the ether chamber, the sutures were gently removed, and a small incision was placed in the midline beneath the wound. The catheter condom was then inserted high in the peritoneal cavity. Layers of the abdominal wall were approximated about the catheter with a heavy braided silk suture. Tensile strength determinations were made on the first, second, third, fifth, and seventh days in both animal groups, and additional determinations were made on the fourth, sixth, and ninth days in the animals which had been receiving the low protein diet. The average base line for the entire experiment was computed from the results which were obtained in 19 rats.

An additional control study was conducted in order to determine the influence of osmotic factors on the healing process. It was thought

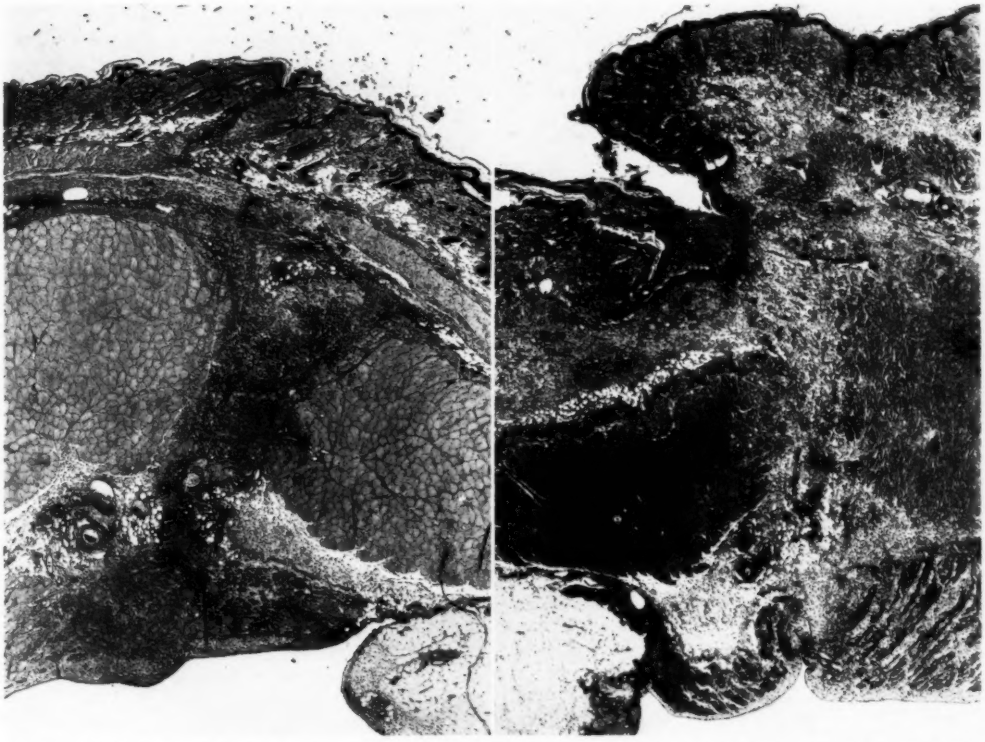


Fig. 3. a, left, Cross section photomicrograph (× 20) of abdominal wall incision of normal control rat on the fifth postoperative day. Fibroplasia and collagen production are occurring with great intensity. b, Cross section photomicrograph (× 20) of abdominal wall incision of protein depleted rat on the fifth postoperative day. Fibroplasia and maturation of reticulum into mature collagen are both delayed.

that the hypoproteinemic rats were in a compensated osmotic equilibrium because they showed no gross edema; however, minor osmotic fluctuations may have been present, and these possibly could have accounted for differences in tensile strength. The rats used in the determination of postoperative caloric intake were maintained on their respective diets for a period of 3 weeks after their initial operation, when they were reoperated upon on the opposite side. A filtered autoclaved solution of 6 per cent gum acacia was administered daily via the tail vein in doses of approximately 1 gram per kilogram of body weight. The latter value amounted to approximately 5 cubic centimeters for the normal animals weighing between 250 and 300 grams and 2.5 cubic centimeters for the animals in the hypoproteinemic group weighing between 120 and 150 grams. Tensile strength determinations were made on the fifth postoperative day.

RESULTS

The results (Fig. 2, Table I) indicate that during the first 2 postoperative days little difference existed between the tensile strengths of wounds in either dietary group. However, on the third day a divergence occurred in the protein depleted animals, with a plateau in the tensile strength curve maintained up to the fifth postoperative day. At this time the normal animals were found to possess a strength approximately 3 times that which was observed in the protein deficient group. Subsequently, the healing proceeded at an al-

most parallel rate, the healing in the protein deficient animals lagging by a period of approximately 2 days.

Adjustment of the plasma oncotic pressure by means of gum acacia appeared to have no effect on the tensile strength of the wounds in either depleted or normal animals. Thus, on the fifth postoperative day, animals on the low protein regimen alone had wounds which disrupted at an average of 62 millimeters of mercury, while the wounds of those on the low protein diet plus intravenous gum acacia separated at an average tension of 65 millimeters of mercury. Animals on the control diet had wounds disrupting at an average tension of 110 millimeters of mercury, while the wounds of control animals receiving gum acacia disrupted at an average pressure of 111 millimeters of mercury.

Although differences in weight between the normal controls and the depleted animals might account for the variation in the tensile strength on a given day, it does not seem likely that these weight differences could account for the overall course of the healing pattern as demonstrated in the respective dietary groups (Fig. 2).

In order to control this factor of body size, observations were made on a series of young, well nourished rats with body weights comparable to the protein depleted animals. In this group as a whole the tensile strength curve showed a consistent rise between the third and fifth postoperative days. On the fifth postoperative day it was found that the tensile strength of the wounds in these smaller animals fell within the range of that of the larger control animals.

Histologic examinations revealed that during the first 2 postoperative days the tensile strength was roughly proportionate to the amount and organization of the fibrin laid down at the line of incision with negligible difference between the protein depleted and control specimens. In addition, there was little evidence of fibroplasia until the third day, except in occasional instances in which early activity was present in the normal control preparations. On the third postoperative day definite fibroplasia was observed, with considerable deposition of reticulum. On the fifth postoperative day (Fig. 3a) it was seen that the fibroblastic number and activity were more pronounced in those animals fed the control ration, with collagen formation and only moderate amounts of reticulum. This was in contrast to the protein depleted group (Fig. 3b) in which fibroblastic activity was obviously depressed. In the latter group reticulum was present to a greater extent along the incision, and cellular response had neither the organization along lines of stress, the density, nor the general maturity noted in the normal animals. Fibroplasia occurred on subsequent days with great intensity in both groups, and collagen formation was particularly pronounced in the normal animals with seemingly only a moderate quantitative cellular difference in the group of animals which were receiving less protein.

Tissue edema was absent and wound infection was not common; however, in the protein deficient rats there was evidence of poorer resistance with occasional instances of abscess formation along the suture channels and occasional diffuse leucocytic infiltration. Epithelial healing was characteristically rapid in both groups with regeneration across the plane of incision by the second day after operation.

COMMENT

Further evidence is offered from these experiments that protein deficiency hampers wound healing. The effect of this deficiency has been shown to result in a characteristic delay in healing from the third through the fifth postoperative days.

In general, however, within the range of protein depletion with which we worked, it was not possible to correlate serum protein levels or percentage weight loss with wound tensile strengths. Higher or lower degrees of an already well marked protein deficiency did not appear to alter the ability of the tissues to heal. A protein depleted rat which had lost 20 per cent of its body weight exhibited as poor healing as its fellow which had lost 40 per cent of its weight. Likewise, rats with serum proteins as low as 3.2 grams per cent produced wounds with as great strength as those in similar animals with serum proteins of 5.0 grams per cent.

It has been claimed by Rhoads, Fleigelman, and Panzer that fibroplasia occurs despite the lowered serum proteins. This finding was corroborated in the present studies by the formation of fibroblasts in both the normal and protein deficient animals. However, although fibroplasia occurred in animals maintained on the low protein diet, it was marked by a delay in its early phases. Furthermore, in acute depletion experiments with maintenance of the oncotic equilibrium it is possible that serum protein levels will not reveal the extent of protein reserves and the ability of the body to regenerate tissue; however, in chronic protein deficiency a lowered serum protein appears in general to indicate tissue protein loss (8) and, in addition, impairment of healing.

An interesting question may be raised: Is the delay in wound healing related merely to the presence of a negative nitrogen balance or is the effect due to exhaustion of the protein reserves coupled with the negative nitrogen balance?

In addition to the loss of circulating and tissue protein, other associated elements undoubtedly contribute to the disturbed healing. In animals rendered hypoproteinemic by plasmapheresis, wound disruption has been shown to occur frequently (9). This result has been attributed to disturbed osmotic relationships and has been prevented by the administration of acacia to maintain oncotic equilibrium (7). The importance of osmotic equilibrium in wound disruption has likewise been emphasized by Koster and Shapiro, and they have stressed particularly the importance of the serum albumin fraction in maintaining a normal osmotic system.

Under the conditions of the present study the animals appeared to be in a relatively normal state of fluid equilibrium. They were not grossly edematous. The ratio of carcass water to carcass protein was not significantly disturbed (2). This was true despite the hypoproteinemia and the large tissue loss. It is possible that this was in part due to the relatively high potassium content of the diet (10) with its resultant diuretic action (2). Thus, it seems unlikely that edema played any major rôle in the retardation of wound healing observed in these protein deficient animals. The experiments in which the colloid osmotic pressure of the plasma of the depleted animals was elevated by the injection of gum acacia substantiate this conclusion.

It should be pointed out, however, that under situations of stress on the fluid regulatory mechanism, such as the sudden flooding of the system with excess fluid and salt, edema is much more likely to occur in the hypoproteinemic animals than in the normal. Such edema will undoubtedly add to the difficulties of repair already present in the protein deficient tissues.

SUMMARY AND CONCLUSIONS

1. A method is described for measuring the tensile strength of wounds of the abdominal wall in small animals.

2. The healing of incised wounds of the abdominal wall of rats is delayed in protein deficient animals.

3. With the onset of fibroplasia on the third postoperative day there is, in general, a marked difference in the tensile strength of the wounds of the animals maintained on the two rations. This difference is most apparent on the fifth day, at which time the wounds of the animals on the normal diet are 3 times as strong as those of the animals on the low protein diet. On subsequent days the strength of the wounds rise in parallel fashion, those of the low protein group lagging by approximately 2 days.

4. The lowered tensile strength of wounds noted in protein deficient rats during the third to fifth postoperative days is apparently due to (a) diminution in the number of fibroblasts, a decrease in their rate of maturation, and a general failure of the fibroblasts to organize with adequate density along the lines of stress; and (b) delay in maturation of the reticulum into mature collagen.

5. No relationship was demonstrated between various concentrations of the lowered blood protein and wound tensile strength, nor with respect to the degrees of weight loss and tensile strength. However, in the presence of serum protein depletion and marked weight loss, the wounds invariably exhibited a characteristic, although moderate, delay in the early phases of fibroplasia.

6. Wounds of rats maintained on an adequate protein diet usually heal cleanly by primary intention, whereas those of rats fed a low protein ration tend to heal with more wound infections and excess wound secretions.

REFERENCES

1. Barbour, H. G., and Hamilton, W. F. J. Biol. Chem., 1926, 69: 625.
2. Benditt, E. P., et al. Unpublished observations.
3. Cannon, P. R., Humphreys, E. M., Wissler, R. W., and Frazier, L. E. J. Clin. Invest., 1944, 23: 601.
4. Clark, A. H. Bull. Johns Hopkins Hosp., 1919, 30: 117.
5. Harvey, S. C., and Howes, E. L. Ann. Surg., 1930, 91: 641.
6. Koster, H., and Shapiro, A. Arch. Surg., 1940, 41: 723
7. Rhoads, J. E., Fleigelman, M. T., Panzer, L. M. J. Am. M. Ass., 1942, 118: 21.
8. Sachar, L. A., Horvitz, A., and Elman, R. J. Exp. M., 1942, 75: 453.
9. Thompson, W. D., Ravdin, I. S., and Frank, I. L. Arch. Surg., 1938, 36: 500.
10. Wissler, R. W., Woolridge, R. L., Steffee, C. H., and Cannon, P. R. J. Immun., Balt., 1946, 52: 267.

PAPILLARY CARCINOMA OF THE THYROID AND LATERAL CERVICAL REGION

So called "Lateral Aberrant Thyroid"

GEORGE CRILE, Jr., M.D., F.A.C.S., Cleveland, Ohio

IN 1939 I reported in this journal a series of 13 cases of papillary tumors of lateral aberrant thyroid origin followed for an average period of 4 years after operation. At that time the literature contained no reports of proved distant metastasis from this type of tumor and in none of our cases had distant metastasis occurred. I concluded, therefore, that these tumors were multiple primary, benign, or locally malignant lesions arising simultaneously in the thyroid and lateral cervical region as a result of some disturbance in the development of the lateral anlage of the thyroid. It did not seem plausible to believe that the lateral cervical nodules, frequently 10 to 20 in number, could represent metastasis from a carcinoma of the thyroid and that at the same time all the patients could be cured by simple removal of the thyroid and lateral cervical tumors. In view of the excellent prognosis it seemed more reasonable to consider these tumors as multiple primary, relatively benign neoplasms.

Eight years have passed and 9 new cases have been added to the list.[1] All 21 of these patients have been followed for from 5 to 20 years or until their death. The survival record of these patients still lends support to the theory that in some cases, at least, the lateral cervical nodules are multiple primary tumors of benign behavior. Yet in 1 case we have incontrovertible proof of the malignancy of these tumors and of their ability to metastasize distantly, and in a second there is strong evidence that this is the case. Similar examples of distant metastasis have been reported by Pemberton (2), Lahey, and others since 1939. In view of the continuing controversy over the true nature of these lesions and treatment of choice, its seems fitting to report the present status of these 21 cases (Table I).

Two patients have died with distant metastases, one to the brain (not proved) and one to the axilla and mediastinum (proved by biopsy). One patient died with a local recurrence of the thyroid tumor. Two have died of other causes, apparently free from cancer 84 months and 59 months, respectively, after operation. One patient, who has had only a biopsy, is alive and well 20 years with multiple tumors in both lobes of the thyroid and throughout both cervical regions. One patient (previously reported) died after operation (1). The remaining 14 patients are alive and well with no evidence of local recurrence or distant metastasis.

The 3 patients who died as a result of recurrence or metastasis of the tumor died 18 years, 15 years, and 9 years, respectively, after their original operations. Similar cases have been reported by others, and hence we must conclude that in dealing with this type of cancer 5 years is no measure of a cure. The thyroid and lateral cervical region of the patient who has persistently refused operation and irradiation for 20 years is filled on each side with nodules ranging in size from 1 to 3 centimeters in diameter. Although the tumors are much more numerous than they were at first, they have never attained such a size as to produce symptoms or a significant visible deformity of the neck. The fact that the number of tumors has increased from 3 to 20 or more suggests metastasis but could be interpreted as the progressive appearance of multiple independent tumors of congenital origin.

One of the 3 patients who have died of carcinoma developed a massive local recurrence 15 years after the original thyroidectomy. Associated with the recurrence was a single lat-

From the Cleveland Clinic.

[1]One has been eliminated because analysis does not indicate with certainty that the nodule was not removed from the thyroid rather than from the lateral cervical region. As this patient had died without recurrence at the time of the previous report it does not materially alter the series.

TABLE I.—SUMMARY OF 21 CASES

Case Age at onset Sex	First symptom and duration before operation	Palpable tumor in thyroid	Preoperative diagnosis	X-ray or radium	Number and type of operation	Number and location of nodules	Bilateral cervical nodule	Bilateral thyroid tumor	Size of thyroid tumor	Operation on thyroid	Location of recurrences	Sclerosis of thyroid tumor	Associated benign adenoma	Pathology	Present status
*1 32 F	Lateral cervical tumor 18 mo.	o	Hodgkins	o	1. Removal nodule	1, Carotid	▪	–	–	o	o	–	–	Papillary adenoma	Died other causes free of recurrence proved by autopsy 59 mo. after operation
2 26 F	Lateral cervical tumor 18 mo.	Firm	Tuberculosis	o	1. Lobectomy neck dissection thyroidectomy incision 2. Removal recurrent nodules	28, low and mid. carotid mediastinal and posterior to thyroid	+	o	2.5 cm.	Complete lobectomy	Mediastinum	o	o	Papillary adenoma	No recurrence 97 mo. postoperative
3 14 F	Lateral cervical tumor 72 mo.	Hard	Correct	Radium seed at op.	1. Lobectomy and neck dissection ant. sternomastoid incision	7, high low and middle carotid and posterior to thyroid	▪	o	2.5 cm.	Complete lobectomy	▪	Bone formation	o	Papillary carcinoma	No recurrence 64 mo. postoperative
4 19 M	Lateral cervical tumor 1 wk.	Hard	Correct	▪	1. Lobectomy and neck dissection left 2. Lobectomy and neck dissection right (ant. sternomastoid incisions) 3. Removal nodules	40 or more bilaterally along carotid from angle of jaw to mediastinum and behind thyroid	+	+	1.5 cm. each lobe with diffuse infiltration	Complete thyroidectomy	Carotid above field of op. at level of jaw angle	▪	o	Papillary carcinoma	No recurrence 64 mo. postoperative
*5 56 F	Lateral cervical tumor 36 mo.	▪	Branchial cyst	▪	1. Removal nodule and part of thyroid (thyroidectomy incision)	1, middle carotid	o	o	–	Incomplete thyroidectomy without examination posterior surface	o	–	+	Papillary adenoma	No recurrence 101 mo. postoperative
*6 53 F	Hyperthyroidism	o	Nodular goiter with hyperthyroidism	o	1. Removal of nodules and part of thyroid (thyroidectomy incision)	3, middle carotid	o	o	–	Incomplete thyroidectomy without examination of posterior surface	o	–	+	Papillary adenoma	Died other causes ("stroke") without recurrence
7 36 M	Tumor thyroid 12 mo.	Firm	Adenoma of thyroid	800 r. after 1st. op.	1. Partial thyroidectomy 2. Complete lobectomy and removal of nodules (thyroidectomy incision)	2, middle carotid	o	o	4.5 cm.	1. Incomplete thyroidectomy 2. Complete lobectomy	Middle carotid	Calcium	+	Papillary adenoma	Died of cerebral metastasis and local recurrence 180 mo. after first operation

TABLE I.—SUMMARY OF 21 CASES—Continued

Case Age at onset Sex	First symptom and duration before operation	Palpable tumor in thyroid	Preoperative diagnosis	X-ray or radium	Number and type of operation	Number and location of nodules	Bilateral cervical nodule	Bilateral thyroid tumor	Size of thyroid tumor	Operation on thyroid	Location of recurrences	Sclerosis of thyroid tumor	Associated benign adenoma	Pathology	Present status
*8 52 F	Lateral cervical tumor	0	Cervical abscess	5450 r. without significant regression or control	1. Removal lateral cervical nodule 2. Partial lobectomy (Thyroidectomy incision)	2, middle carotid	0	0	4.5 cm.	Partial lobectomy; impossible to remove all of tumor	Thyroid	0	–	Papillary adenoma	Died of local recurrence 112 mo. postoperative
*9 16 F	Lateral cervical tumor 72 mo.	None at first, now bilateral hard	Tuberculosis	80% erythema dose in 3 treatments without improv.	1. Biopsy	Only 2 of many removed, 20 or more now palpable	+ palpable, no operation	+ palpable, no operation	Estimated 1–2 cm.	0	Bilateral high and low jugular	–	–	Papillary adenoma	Alive and well with multiple small tumors throughout thyroid and lateral cervical region. Has had no treatment. Now 249 mo. since biopsy and 27 yr. since tumors were first noticed
10 27 F	Lateral cervical tumor 2 mo.	Enlarged right lobe	Correct	0	1. Lobectomy and neck dissection (anterior sternomastoid incision) 2. Removal nodule	20 or more Entire length of carotid, mediastinum behind thyroid; 1 nodule other side	1 on the other side	0	3 cm. diffuse infiltration	Complete lobectomy	2 yrs. postop. noted tiny nodule in midline above thyroid; removed 8 yrs. postoperative, 1 cm. diameter	Calcium	+	Papillary adenoma	No recurrence 108 mo. after operation
11 15 F	Lateral cervical tumor 36 mo.	0	Correct (previous biopsy)	4000 r. with only transient regression followed by continued growth	1. Biopsy (elsewhere) 2. Removal nodules 3. Removal nodules and lobectomy 4. Removal nodules and tumor in other lobe (Thyroidectomy incision)	15, low carotid, mediastinum and posterior to thyroid, bilateral	+	+	1 cm. each lobe	Tumors removed from both lobes of thyroid	Low carotid and mediastinum	Scar	0	Papillary adenoma	No recurrence 115 mo. since first operation and 72 mo. since last
12 28 F	Lateral cervical tumor 30 mo.	Firm	Correct	0	1. Biopsy (elsewhere) 2. Lobectomy and removal of nodules (Thyroidectomy incision)	4, middle carotid	0	0	2 cm.	Complete lobectomy	0	Calcium	+	Papillary adenoma	No recurrence 83 mo. since operation

TABLE I.—SUMMARY OF 21 CASES—Continued

Case Age at onset Sex	First symptom and duration before operation	Palpable tumor in thyroid	Preoperative diagnosis	X-ray or radium	Number and type of operation	Number and location of nodules	Bilateral cervical nodule	Bilateral thyroid tumor	Size of thyroid tumor	Operation on thyroid	Location of recurrences	Sclerosis of thyroid tumor	Associated benign adenoma	Pathology	Present status
13 9 F	Tumor thyroid 12 mo.	Hard	Correct	0	1. Lobectomy and dissection lower neck (Thyroidec. incision) 2. Removal nodules	6, middle carotid	0	0	2.5 cm.	Complete lobectomy	1 yr. postoperative noted tiny nodule left carotid. Enlarged slowly, removed 7 yrs. later	0	+	Papillary adenoma	No recurrence; well 97 mo. after operation
*14 33 F	Tumor in thyroid 144 mo.	Goiter (no description)	Adenoma	0	1. Thyroidectomy 2. Removal nodules 3. Removal nodules (all in 3-mo. period)	8, middle carotid	0	0	3 cm.	Partial thyroidectomy	Persistent tumors in middle-carotid area removed 1 wk., 3 mo. after thyroidectomy	Calcium	+	Papillary adenoma	No recurrence 206 mo. postoperative
*15 21 F	Lateral cervical tumor 12 mo.	0	Tuberculosis	X-Ray ? amt.	1. Removal nodules 2. Removal nodules and lobectomy	3, middle carotid	0	0	1.5 cm.	Partial lobectomy	Thyroid tumor and nodules middle-carotid area removed 6 yrs. after 1st operation	Scar	+	Papillary carcinoma	No recurrence 124 mo. after first 24 mo. after 2nd operation
16 24 F	Lateral cervical tumor 1 wk.	0	Correct (previous biopsy)	0	1. & 2. Removal nodule 3. Removal nodule 4. Removal nodule, 5 & 6 (?) Removal of nod. (elsewhere)	4+ ? low carotid	0	0	—	0	Tumors keep recurring low carotid area	—	—	Papillary adenoma	Living and well 168 mo. since original operation but is said to have had recurrences removed since last operation at Cleveland Clinic
17 38 M	Lateral cervical tumor 12 mo.	Hard	Correct	0	1. Removal nodules 2. Neck dissection and lobectomy (ant. sternomastoid incision)	25, along carotid, and mediastinum	0	0	3.5 cm.	Complete lobectomy	2nd operation 6 wk. after 1st.	Calcium	0	Medullary carcinoma with invasion of veins; frankly malignant	No recurrence 113 mo. postoperative
18 43 M	Tumor in thyroid 4 year duration	Hard	Correct (previous op.)	17 treatments amount unknown, no improvement	1. Thyroidectomy (elsewhere) 2. Complete lobectomy and block dissection of neck	13, along carotid, posterior to thyroid and in mediastinum	+	0	3.5 cm.	Complete lobectomy	Contralateral and in mediastinum and thyroid and carotid area	0	+	Papillary carcinoma	Died after 2nd operation. First operation was 10 yrs. before

TABLE I.—SUMMARY OF 21 CASES—Concluded

Case Age at onset Sex	First symptom and duration before operation	Palpable tumor in thyroid	Preoperative diagnosis	X-ray or radium	Number and type of operation	Number and location of nodules	Bilateral cervical nodule	Bilateral thyroid tumor	Size of thyroid tumor	Operation on thyroid	Location of recurrences	Sclerosis of thyroid tumor	Associated benign adenoma	Pathology	Present status
19 20 F	Lateral cervical tumor 24 mo.	Hard	Tuberculosis	12 treatments amount unknown, no improvement	1. Removal nodules 2. Bilateral lower neck dissection (Thyroidectomy incision)	12, mediastinum, behind thyroid bilateral middle carotid	+	+	3 cm. one lobe. 1 cm. other	Complete lobectomy on right partial on left	Bilateral carotid, mediastinum and thyroid	Calcium	+	Papillary carcinoma	No recurrence 175 mo. after first and 3 mo. after 2nd operation
39 48 F	Lateral cervical tumor 30 mo.	0	Correct	7 treatments amount unknown, no improvement	1. Neck dissection and lobectomy	5, middle carotid and mediastinum	0	0	1 cm.	Complete lobectomy	0	Calcium	+	Papillary carcinoma	No recurrence 60 mo. postoperative
21 33 M	Tumor thyroid 24 mo.	Hard	Correct	Large amount, no improvement	1. Thyroidectomy 2. Excision nodule and lobectomy	1, Posterior triangle	0	0	Very large	Complete lobectomy	Local recurrence thyroid nodule in posterior triangle	+	0	Papillary adenoma	Died with axillary and mediastinal metastasis (proved) 227 mo. after operation

eral cervical nodule, grossly and histologically identical to the tumors that in the past we have called lateral aberrant thyroids. There was present in this case the rich pedicle of blood vessels so characteristic of the lateral aberrant thyroids and so different from the blood supply of other types of metastases in lymph nodes. Yet metastatic carcinoma histologically identical to that seen in the thyroid and lateral cervical region was later found in the axilla. It is inconceivable that axillary thyroid tissue could be of congenital origin. The patient died 4½ years after the second operation and over 19 years after removal of the original papillary tumor.

The second patient was reoperated upon for a local recurrence of the thyroid tumor 9 years after the original operation, and again a single lateral cervical nodule, grossly and histologically similar to those described as lateral aberrant thyroids, was found. Six years later (15 years after the original carcinoma of the thyroid was removed) this patient died, apparently with cerebral metastasis, although a postmortem examination was not done.

The third patient developed a large carcinoma of the thyroid which appeared a few months after a lateral cervical nodule was removed. In spite of x-ray therapy she died with local recurrence of the tumor 9 years after the original operation.

The remarkable survival record of the other patients with or without surgical removal of the tumors is demonstrated in the table.

The ability of these tumors to metastasize, as shown by the reports of Pemberton (2), Lahey, and others and by the progress of our patients since they were reported in 1931, indicates that regardless of their histology and regardless of their relatively benign clinical behavior, these tumors must be considered malignant. Yet they must be considered in a separate category of malignancy, one in which metastasis is recognized yet cognizance is taken of the usual tendency to grow extremely slowly. They can be characterized as having the following qualities:

1. A marked tendency, regardless of histologic criteria of malignancy, to metastasize locally to the glands of: (a) the lower and mid-cervical region behind and about the carotid

sheath, (b) the region posterior to the thyroid along the trachea and along the course of the recurrent nerve, (c) the superior mediastinum, (d) the posterior triangle of the neck, (e) the upper part of the neck in relation to the carotid sheath, (f) the midline along the thyroglossal tract, (g) possibly contralaterally, although usually a second primary tumor in the other lobe is demonstrable.

2. A slight tendency to metastasize distantly (a) via the blood stream, especially to the lungs, (b) via the lymphatics to the axilla.

3. A marked tendency for the tumor in the thyroid to calcify, scarify, or even to ossify, the primary tumor often failing to enlarge significantly over a period of many years in spite of the fact that its metastases may show steady growth and increasing numbers.

4. A tendency for the lateral cervical metastases to grow only slowly over a period of many years and to remain encapsulated, noninvasive, and freely movable.

A primary tumor has been found in the thyroid gland of every one of 16 consecutive cases in which I have explored the thyroid or removed one of its lobes. Aside from the 4 tumors that we have observed in both lobes of the thyroid, all others in the thyroid proper have been single primary tumors. In 3 cases the tumor has infiltrated the gland more or less diffusely, forming an adenopapillomatous infiltration of the affected lobe, but in no cases has there been more than one distinct tumor nodule in a lobe of the thyroid. The fact that in the 16 consecutive patients whose thyroids I have explored there have been multiple lateral cervical nodules and only one nodule in the lobe of the thyroid would seem an argument against the hypothesis that the tumor in the thyroid is, as some believe, a metastasis from a primary malignancy in the lateral cervical region. These observations tend to substantiate Pemberton's theory that most, if not all, of the lateral cervical nodules are metastases of a carcinoma primary in the thyroid.

Against this view we have 5 patients followed for from 5 to 14 years after removal of a lateral cervical nodule who have never developed any palpable tumor in the thyroid. That this does not rule out the presence of a primary tumor in the thyroid is illustrated by an additional case in which 6 years intervened between the removal of a lateral cervical nodule and a second operation for recurrent lateral cervical nodules. Prior to the second operation, no tumor was palpable in the thyroid, yet at the time of the second operation a tumor 1.5 centimeters in diameter was found in the lobe on the affected side. The tumor was surrounded by much dense scar tissue. It is quite likely, therefore, that many of the primary tumors in the thyroid enlarge little at all over a period of many years and so may escape detection unless they are searched for. Yet these same tumors may, as in this case, continue to give rise to actively growing metastases while the primary tumor fails to enlarge.

Experience has shown that even a partial lobectomy does not rule out the presence of a small primary tumor. I have recently removed a papillary carcinoma of the thyroid and a number of lateral cervical nodules a little over a year after a "thyroidectomy" had been performed. At the time of the first operation neither the surgeon nor the pathologist was aware of the presence of this tumor which, as is so often the case, lay on the posteromedial aspect of the thyroid, an area avoided by many surgeons. On another occasion before I became aware of the significance of the lateral cervical nodules in respect to the thyroid tumor, I explored the thyroid of a girl with lateral cervical nodules and reported it normal, only to reoperate for recurrent cervical nodules a year later and find that there was indeed a tiny nodule less than 1 centimeter in diameter on the posteromedial aspect of the thyroid. Thus failure to demonstrate a tumor in the thyroid at operation or in the portion of the gland removed does not by any means rule out the possibility that a tumor in the posteromedial remnants was overlooked.

The extreme slowness of growth of certain of the tumors in the thyroid is illustrated by the case of a girl 20 years old whose thyroid contained a nodule estimated to be 1.5 centimeters in diameter. Lateral cervical nodules were removed, but the thyroid tumor was not disturbed. Fifteen years later more lateral cervical nodules and the thyroid tumor were removed, but after all these years the tumor

in the thyroid was only 2 centimeters in diameter. The fact that no tumor appears in the thyroid even 10 or 15 years after removal of lateral cervical nodules does not therefore prove that there is no primary tumor in the thyroid. It means only that in all probability the tumor in the thyroid is very small, lies deep on the posterior surface of the gland, and is either growing very slowly or its growth is prevented by calcification and scarring.

One of the most significant features of these tumors is the fact that in every one of the 16 patients with lateral cervical nodules whom I have explored I have found a tumor in one or both lobes of the thyroid. The fact that in 5 cases tumors were found in both lobes of the thyroid suggests that the thyroid tumors originate in some congenital rest or anomaly of development. The youth of the patients (6 had developed lateral cervical nodules by the age of 20) also suggests a congenital origin, as does the histologic appearance of some of the cervical nodules. Yet in other cases the lateral cervical nodules are clearly metastases in lymph nodes, and it is therefore reasonable to assume that most if not all of the lateral cervical nodules are metastases from the thyroid.

Regardless of the origin of these tumors or of their classification in respect to malignancy, their treatment should be surgical excision. It is indeed a strange type of cancer that can be controlled for 15 or 20 years by local excision of the primary tumor and individual removal of 15 or 20 or more metastatic nodules. It is also a curious type of malignancy which, without any form of treatment, grows so slowly that in over 20 years the nodules have not enlarged appreciably and have merely become more numerous. It is almost as if these tumors were metastasizing congenital rests having little or no energy of growth. Yet in other cases the tumors enlarge fairly rapidly and sometimes attain considerable size. When the primary tumor of the thyroid rather than the lateral cervical nodules is noticed first, the growth energy appears to be greater. Three of the 4 patients who eventually died as a result of tumor developed a bulky tumor of the thyroid as the initial symptom. There were only 2 other patients in the entire group whose thyroid tumors were noticed before the lateral cervical nodules. The patients whose initial symptoms are referable to bulky tumors of the thyroid and in whom lateral cervical nodules are late developments should perhaps be placed in a different category from those in whom the lateral cervical nodules are the initial and most striking manifestations of the disease.

Complete removal of the tumors involving the posteromedial aspect of the thyroid and of the metastatic nodules along the trachea and the course of the recurrent nerve is often very difficult. The scarring and calcification of the tumors in this location render them adherent and often make it difficult to identify, isolate, and preserve the recurrent nerve. If a meticulous dissection of the nerve is made, however, it is usually possible to preserve it. Often it is necessary to isolate and dissect out the entire cervical portion of the nerve. Even when it is adherent to the tumor it may be possible to separate it from the mass without either leaving tumor tissue or damaging the nerve. On several occasions it was impossible to save the nerve without leaving tumor tissue, and hence after dissecting it out it was necessary to sacrifice it. When the choice lies between sacrifice of the nerve and removal of all tumor the nerve should be sacrificed.

It is apparent from the table that most of the patients in this series have had more than one operation and that some have had three. All of the patients who have had three operations were operated upon early in our experience before we were aware of the fact that a tumor is usually if not always present in the thyroid. Metastasis, therefore, continued to occur from the thyroid tumor until it was removed.

Even after the importance of the thyroid tumor was recognized, many of the patients with 15 or more lateral cervical nodules required a second operation for removal of one or more overlooked nodules. In several instances the recurrence was contralateral or mediastinal and in one it was in the thyroglossal tract. In only 1 case was the recurrence in the field of the first operation, and only in this case would a block dissection of the neck have eradicated the tumor more completely than mere removal of the nodules.

In most of the patients the recurrences were first noticed within a few months of the first operation, and most of these patients were operated upon promptly and have remained well for from 5 to 10 years. In 2 instances the recurrences were noted early, but operation was deferred as the result of the war for 4 or 5 years. The nodules enlarged only very slowly and no more nodules developed, again suggesting that if the source of the trouble in the thyroid is eradicated the tendency for additional lateral cervical nodules to develop is controlled.

CASES ILLUSTRATING SLOWNESS OF GROWTH

A patient was seen in 1925 complaining of lumps in the neck of 6 years' duration, first noticed at the age of 16. Several large soft glands were palpable in the left lateral cervical region. A diagnosis of tuberlous adenitis was made. Three x-ray treatments (2 with 30 per cent erythema dose and 1 with 20 per cent) were given without benefit. A biopsy was reported as revealing metastasis of a papillary carcinoma of the thyroid or an aberrant papillary adenoma of the thyroid. The patient refused further treatment. In 1939, 14 years later, the patient had a hard tumor 2.5 centimeters in diameter in the left lobe of the thyroid, a hard tumor 2 centimeters in diameter in the midline above the isthmus, as well as a tiny hard nodule in the right lobe of the thyroid and numerous lateral cervical nodules beneath the sternomastoid on each side. None of these nodules was large enough to be visible except the one above the isthmus. In 1946, 21 years after biopsy and 27 years after the nodules had first been noticed, the patient writes that she has no symptoms referable to the tumors and has "only one small tumor" in the front of her throat.

A woman, aged 21, first noted "glands" in the right side of her neck a year before entry. There was a large, round, fluctuant, cystic mass 6 centimeters in diameter at the base of the neck on the right under the sternomastoid. There was a firm nodule 1.5 centimeters in diameter in the superior pole of the right lobe of the thyroid and two firm round masses 2 centimeters in diameter under the sternomastoid on the right. A diagnosis of tuberculous adenitis or branchial cyst was made. Eleven light x-ray treatments were given without improvement. Four of the lateral cervical masses were removed and the pathologist reported multiple cervical papilliferous cysts of the lateral aberrant thyroid. The thyroid was not explored. The patient returned 14 years after operation and more than 16 years from the time the tumor was first noticed. She had no symptoms referable to the cervical tumors, but examination revealed a hard nodule 2 centimeters in diameter at the right lobe of the thyroid and bilateral cervical nodules. The left lobe of the thyroid seemed normal.

At operation there was a partly calcified papillary carcinoma of the right lobe of the thyroid gland 3 centimeters in diameter and a similar tumor 1 centimeter in diameter in the left lobe. There were 8 lateral cervical nodules, some present on each side in the neighborhood of the thyroid as well as posterior to the carotid sheath and in the superior mediastinum. Convalescence was uneventful, and 3 months later there was no evidence of recurrence. This case is interesting because it shows how long these tumors can be present in the thyroid without enlarging appreciably or causing symptoms other than those referable to the lateral cervical metastases. It also indicates that, as was the case in the left lobe, a tumor may be present without being palpable prior to operation.

CASES SHOWING THAT METASTATIC NODULES MAY CONTINUE TO DEVELOP UNTIL THE PRIMARY TUMOR IN THE THYROID IS REMOVED

A girl, aged 18, had noticed lumps in the right lateral cervical region for 3 years. Later similar lumps developed on the left side and enlarged steadily. A biopsy of one of the lumps was reported as metastatic adenocarcinoma. Twenty-one x-ray treatments with a total of 4000 r units were given, and the nodules decreased slightly in size for a few weeks and then began to enlarge again. Examination revealed nodules 3 centimeters in diameter beneath the sternomastoid on each side, but no abnormality of the thyroid was noted. Through a thyroidectomy incision Dr. George Crile, Sr., removed 5 cystic nodules from the region of the carotid sheath on each side. One of the tumors was removed from the mediastinum at the level of the arch of the aorta. The thyroid was examined and reported as normal. The pathologist reported the tumors as multiple benign intracystic papillomas of lateral aberrant thyroid origin.

Six months later the patient noticed a recurrent tumor in the right lateral cervical region. Examination showed several small firm nodules behind the lower part of the sternomastoid on the right and an enlargement of the left lobe of the thyroid. At operation a tumor 3 centimeters in diameter was removed from the region of the carotid sheath on the right. The left lobe of the thyroid containing a tumor 1 centimeter in diameter also was removed. The right lobe of the thyroid was examined and found to be normal. The pathologist reported a small localized papillary adenomatous growth in the left lobe of the thyroid. It was thought that this tumor and the lateral cervical nodule, which was of similar histology, were both benign.

The patient remained well for 3 years and then developed a small firm nodule in the right lobe of the thyroid 1 centimeter in diameter. At operation the right lobe of the thyroid containing a small tumor was removed, and 9 separate nodules were removed from the lateral cervical region and superior medi-

astinum. The pathologist again reported papillary adenomas of the thyroid and of lateral aberrant thyroid origin.

It is over 6 years since the last operation and the patient has had no further recurrences. It was not until the 2 primary tumors in the thyroid were resected that the lateral cervical nodules stopped forming.

A woman, aged 29, had developed a lump in the right side of her neck 5 years before entry. In 1932 Sir John Fraser had removed aberrant thyroid tissue from the right side of her neck at the Royal Infirmary, Edinburgh, Scotland. Shortly after operation the lump reappeared. It was again removed in 1936.

Examination showed a nodule 2.5 centimeters in diameter beneath the lower part of the sternomastoid on the right. The thyroid was normal.

In 1937 Dr. George Crile, Sr. removed a nodule from the region of the carotid sheath low on the right. It was reported as a cystic papillary adenoma of lateral aberrant thyroid.

A month later another tumor was noticed in the same location, and 5 months later 3 papillary adenomas were removed from the same region. A month later there were no masses palpable in the lateral cervical region, but a tiny nodule could be felt in the thyroid gland. The patient returned to England but her sister informs us that the patient has had several more nodules removed from her neck. It is now 15 years since the onset. I do not doubt that she will continue to form nodules until the primary tumor in the thyroid is removed.

CASES ILLUSTRATING GOOD PROGNOSIS IN SPITE OF EXTENSIVE METASTASIS

The following cases in which there were 20 or more lateral cervical nodules illustrate the excellent prognosis (at least for the first 5 or 10 years) which may follow surgical removal of the primary tumor in the thyroid and lateral cervical nodules, regardless of their number and distribution.

A boy was first seen at the age of 10, at which time he had a soft diffuse enlargement of the thyroid which was treated as an adolescent goiter by administration of iodine. The thyroid was examined repeatedly for the next 9 years, and no abnormality of the thyroid other than a slight diffuse enlargement of the entire gland was noted.

At the age of 19 he developed nodules in both lateral cervical regions from the angle of the jaw to the clavicle and a hard nodule the size of a pea in the right lobe of the thyroid. A diagnosis of carcinoma of the thyroid with metastasis was made, and through anterior sternomastoid incisions dissections of the neck were performed without removal of either jugular vein or sternomastoid muscle. There were tumors in both lobes of the thyroid. All of the right lobe and almost all of the left lobe were removed. Numerous lateral cervical nodules, estimated at over 20 on each side, were removed from the region posterior to the thyroid from the superior mediastinum and from along the entire length of the carotid sheath. One month later 2 nodules were noted beneath the angle of the jaw on the right at the upper aspect of the previous operation. These were removed. The pathologist reported papillary carcinoma of both lobes of the thyroid with bilateral metastasis to the cervical glands. The tissue was very cellular, having some tendency to form glands, papillomatous growths, and large solid masses of closely packed cells. The patient has remained well and free of recurrence for over 6 years, and x-ray examination of the chest shows no abnormalities.

Three other patients with extensive thyroid and lateral cervical involvement by carcinoma, each of whom had 25 or more lateral cervical nodules and one of whom had a frank malignancy with invasion of veins by the tumor, are well from 8 to 10 years following operation. These are Cases 1, 2, and 4 reported previously in this journal (2, 3).

It is clear, therefore, that the prognosis in these cases is not entirely dependent either on the histologic appearance of the tumor nor on the extent of the lateral cervical matastasis. The 4 patients who have died as the result of papillary tumors of the thyroid with lateral cervical nodules all had tumors which were originally reported as benign from a histologic standpoint, and in 3 of the 4 cases metastasis to the lateral cervical region did not appear for many years. It is urged, therefore, that regardless of the extent of the lateral cervical metastasis and regardless of the apparent malignancy of the lesion, papillary tumors in the thyroid, lateral cervical region, and mediastinum should be removed surgically. Since none of the 3 patients in this series who had adequate x-ray treatment showed either primary regression or permanent control of the tumor, x-ray cannot always be relied upon to control this type of cancer. We have reserved its use for those cases in which surgery has failed.

SUMMARY

1. Twenty-one cases of papillary carcinoma of the thyroid and lateral cervical region are reported.

2. All patients have been followed from 5 to 21 years or until their death, and only 3 have

died from cancer, 1 with local recurrence in the thyroid and 2 with distant metastasis.

3. The patients who died of cancer lived for 9, 15, and 19 years, respectively, after the original thyroidectomy.

4. One patient who has refused all treatment is living and well 27 years after the appearance of lateral cervical nodules and 21 years after these nodules were proved to be papillary tumors of the thyroid.

5. In judging the results of treatment of papillary carcinoma of the thyroid the usual 5 year period is meaningless. Twenty or more years may be required before one can be sure that the patient is cured.

6. In 16 consecutive cases with papillary tumors of the lateral cervical region, when the thyroid was carefully examined, a primary tumor in the thyroid was found.

7. It is thought that the lateral cervical nodules are probably metastases from a tumor of the thyroid rather than, as I previously believed, primary tumors of congenital origin.

8. Lateral cervical tumors may continue to form until the primary tumor in the thyroid is removed. Following this no more lateral cervical nodules appear.

9. In the few cases in which x-ray has been given, the results have been disappointing.

10. The results of excision of the primary tumor and the lateral cervical and mediastinal metastases have been excellent. Four patients who had 20 or more lateral cervical and mediastinal nodules are well and free of recurrence for from 6 to 10 years after operation.

11. The lateral cervical nodules rarely invade muscles or blood vessels, and block dissection of the neck is therefore not necessary. Since most of the patients are young women, whose necks one would hesitate to mutilate needlessly by a block dissection, it is an advantage to perform the operation through a thyroidectomy incision or, in the more extensive cases, through an incision parallel to the sternomastoid.

12. The tumor in the thyroid may be very small and often is not palpable before operation. On several occasions it was not found until the gland was rotated up out of its bed to expose the posteromedial surface.

13. The tumor in the thyroid usually is scarred or calcified and may not enlarge appreciably over a period of many years in spite of the fact that it continues to give rise to lateral cervical metastases.

14. Regardless of the histology of the tumors and regardless of their apparent hopelessness as suggested by the extent of metastasis, the primary tumor in the thyroid and the lateral cervical and mediastinal metastases should be excised.

REFERENCES

1. Crile, George Jr. J. Am. M. Ass., 1939, 113: 1094–1097.
2. King, W.L.M., and Pemberton, J. deJ. Surg. Gyn. Obst., 1942, 74: 991–1001.
3. Lahey, F. H., and Ficarra, B. J. Surg. Gyn. Obst., 1946, 82: 705–711.

COMMON AND UNCOMMON PATHWAYS IN THE SPREAD OF TUMORS AND INFECTIONS

ERNEST LACHMAN, M.D., Oklahoma City, Oklahoma

THE rationale of surgical intervention in the spread of tumors and infections is by necessity based on a knowledge of the pathways for the propagation of these noxious agents. This is where the anatomist enters the field. It is his function, in co-operation with the pathologist, to map out the channels along which the spread takes place. As different as their pathology is, the avenues along which cancers and infections travel, are essentially the same, namely, the blood and lymph channels. This is the reason why the two disease entities have been combined in the title of this paper. It is certain that we have here a very fruitful field for anatomical research and that many of the peculiarities of metastatic distribution can be explained only on the basis of circulatory anatomy. Selected chapters in the field of cancerous and infectious spread will serve to illustrate the relevant points.

EMISSARY VEINS AS PATHWAYS OF INFECTIONS

Among the pathways of infections, that have become of interest lately, are the veins that connect the venous system outside the skull with the venous sinuses on the inside. There is a rich venous network in the face, the infratemporal region, and around the pharynx which in some places assumes the configuration of venous plexuses, such as the pharyngeal and pterygoid plexuses. These extracranial veins anastomose through foramina of the skull with the large venous channels that are formed by the dura, the dural venous sinuses. What is the function of these connecting or emissary veins as they have been called? They act as safety valves in case of increased intracranial pressure. The connection of the internal jugular vein, which drains these venous sinuses, with the right heart is close enough so that pressure changes in the thorax due to coughing, sneezing, straining, muscular exertion, and forced expiration are readily transmitted to the internal jugular vein and through it to the dural sinuses. This would lead to an abnormal increase in intracranial pressure if it were not for the emissary veins acting as safety valves. We have to visualize in these veins a to and fro movement of the blood, the direction of which depends on the changing pressure conditions in the internal jugular vein. The sinuses and most of the facial veins are devoid of valves, a factor which facilitates the reversal of the blood stream.

On the other hand the tortuosity of the lateral sinus and of the beginnings of the internal jugular vein as well as the meshwork of septa in some of the sinuses act as a check mechanism preventing too much suction on the sinuses in case of a rise in negative pressure in the large intrathoracic veins. These same factors are also responsible for a slowing of the blood flow in the sinuses which might account for the frequent occurrence of aseptic sinus thrombosis. But more dangerous than the sterile type is the septic thrombosis of the sinuses which is transmitted to them by way of the emissary veins. We know how readily infection of the lips and nasal area may lead to cavernous sinus thrombosis which before the advent of chemotherapy was almost invariably fatal. It is the easy reversibility of the venous blood flow in the absence of valves and the milking motion of the ever constricting muscles of facial expression around the veins that are responsible for the dislodgment of a septic thrombus and its passage into the dural sinus. Or an infectious thrombophlebitis in the labial veins may spread by continuity into the angular and ophthalmic veins and from there into the cavernous sinus, leading to sinus thrombosis and meningitis or generalized sepsis. Infection of the orbit and of the frontal and ethmoidal paranasal sinuses

From the Department of Anatomy, The University of Oklahoma School of Medicine. Presented at the meeting of the Oklahoma County Medical Society, May 28, 1946.

may travel the same path. Peritonsillar infection may cause thrombophlebitis of the pharyngeal plexus and spread from there by way of emissary veins through foramina in the base of the skull likewise to the cavernous sinus. Erysipelas of the scalp may infect the superior longitudinal sinus through the parietal emissary vein. Most common is the involvement of the sigmoid sinus in mastoid infection which may spread to the sinus by way of a thrombophlebitis of the middle ear veins, by way of the lymphatics or by continuity directly from the infected mastoid bone (Braun). The emissary veins are also responsible for the fact that spread of infection from the dural sinuses into the general circulation cannot be prevented with certainty by ligation of the internal jugular vein, since the infection may by-pass the ligated vein by way of emissary veins in the region of the occiput which communicate with veins of the neck.

Attention has been called to an "otitic hydrocephalus," complicating middle ear infection (Symonds, 1931). The condition, characterized by bilateral papilledema and severe headaches, results from an increase in intracranial pressure which is brought about by an infection of the sigmoid sinus and by spread of this infection to the superior longitudinal sinus. It is not so much the thrombosis of this sinus, but rather the thrombophlebitis, i.e., the infection of the sinus, which interferes with the absorption of the spinal fluid through the arachnoid villi and leads to rise in intracranial pressure (Symonds, 1937). Symonds (1940) showed that infection in the neighborhood of the tonsils and in the nasopharynx may also lead to hydrocephalus by secondary involvement of the superior sagittal sinus. Thrombophlebitis of this sinus may then spread in retrograde direction into the superior cerebral veins which drain into this sinus and which supply the motor area of the brain. The results are cortical symptoms such as focal epilepsy and hemiplegia. Lately Martin has described a combination of increased intracranial pressure and focal signs of cortical involvement such as convulsions and hemiplegia occurring in the first weeks of the puerperium. The disease may lead to recovery or death. The interesting point is that these so-called thromboses of the venous sinuses and cerebral veins are actually emboli that by a devious pathway have been transported to the brain from pelvic veins, by-passing lungs and other organs. This newly described avenue will be dealt with in later parts of this paper. Here it may suffice to point out that there is an important anastomosis between the veins of the vertebral canal and the dural sinuses through the great occipital foramen.

LYMPHATIC SPREAD OF CANCER OF THE BREAST

Having presented a location which exemplifies the venous spread of infection, it may be appropriate to turn to another mode of propagation, namely, the lymphatic pathway, and select a malignancy for illustration. An ideal representative is cancer of the breast, because it is so easily accessible to surgery and anatomical study. It was this location of cancer for which Sampson Handley developed his theory that cancer spreads centrifugally in all directions from its point of origin by permeation, i.e., continuous invasion of lymphatic plexuses. While Handley's theory of continuous lymphatic spread to distant points in the organism is too dogmatic and narrow, since it disregards lymphatic embolism and venous propagation of cancers, it nevertheless placed the operative treatment of cancer on a rational, i.e., anatomical basis. It laid the scientific foundation for the radical surgical treatment of cancer of the breast which had been developed previously by Halsted on an empirical basis. Halsted's operation exemplified the fact that cancer can be cured even after it has spread from its primary focus to the regional lymph nodes, an experience which is borne out in other locations.

Since the pathways of metastatic spread of mammary cancer were discussed in detail in a previous paper (Lachman), only those facts shall be pointed out here that can be applied also to other areas where lymphatics are involved in the propagation of tumors. The principal lymphatic drainage of the breast passes from its subareolar plexus to the pectoral, central, and apical nodes of the axilla, and from there with or without interposition of supraclavicular nodes into the thoracic duct on the left or the right lymphatic duct. But

deviations from this basic arrangement frequently occur, consisting in short-cuts which may by-pass one, two, or even three of the relay stations mentioned. Thus direct lymph drainage from the breast into the central, apical, or supraclavicular set may occur. In the latter case we have the clinical picture of enlarged supraclavicular nodes without involvement of the axilla, a condition which in general is regarded as inoperable.

Radical surgery with removal of the two pectoralis muscles is predicated on the presence of a direct lymphatic channel from the superior portions of the breast to the apical nodes through the substance or along the deep surface of these muscles. Pressure on nerves in the axilla by enlarged nodes and interference with the lymph drainage of the arm resulting in edema are interesting by-products of axillary metastasis which find their counterpart in nerve symptoms and edema in cancers of other regions.

Another clinically important point is illustrated in the opening up of atypical lymph channels after blockage of the usual lymphatic pathways. This is exemplified by occasional involvement of the inguinal lymph nodes in cancer of the breast. Of the greatest practical importance are pathways from the medial half of the breast to the other breast, to the other axilla, and to the internal mammary nodes. Spread to these locations usually precludes surgical cure. The last named lymph nodes fortunately atrophy in older age thus eliminating this mode of cancer spread. The pleura and peritoneum are within reach of direct lymphatic involvement, the pleura by communications with the lymphatics of the pectoral and intercostal muscles, the peritoneum by way of lymphatics from the inferior and medial segment of the breast, that anastomose through the linea alba with subperitoneal lymph plexuses.

PORTAL VEIN AND LYMPHATICS IN THE PROPAGATION OF TUMORS AND INFECTIONS OF THE GASTROINTESTINAL TRACT

So far we have presented avenues that illustrate the spread of infections in the venous system and of tumors through the lymphatic system. By contrast the portal circulation exemplifies a pathway that is traveled by tumors and infections alike. It is one of the great natural highways along which infections and cancerous emboli may readily pass. Three unpaired arteries supply the gastrointestinal tract and its glands from the lower end of the esophagus to the upper portion of the rectum: the celiac, the superior and inferior mesenteric arteries. They ramify into smaller and smaller arteries and arterioles and finally break up into a capillary network in the wall of the intestines or within the glands. The blood then is collected by venules, which drain into larger and larger veins finally to form the splenic, the superior and inferior mesenteric veins. Their blood is poured into the portal vein which enters the liver and here forms another capillary system around the columns of liver cells. The portal vein thus drains an area in which infections as well as malignancies are very common. Among the infections, appendicitis, ulcerations of the stomach, duodenum, and colon, and diseases of the rectum such as proctitis and infected hemorrhoids, deserve mention. It is particularly appendicitis which may lead to suppurative thrombophlebitis, first, of the tributaries of the portal vein and then of the portal vein itself. The incidence of portal thrombophlebitis in appendicitis varies according to Ochsner from 0.1 to 1 per cent of all cases. The pathway to the portal vein is by way of the appendiceal vein in the mesenteriolum of the appendix, the ileocecal vein and the superior mesenteric. Either by continuous growth of the septic thrombus along the venous channels into the liver or by detachment of a septic embolus from a thrombus in any of the veins mentioned, single or multiple liver abscesses result. Septic embolism in the liver from a phlebitis in the appendiceal vein may occur without involvement of the intervening veins. Abscesses following appendicitis are usually multiple and are located in the right lobe of the liver. It has been pointed out, originally by French authors and later by others in this country, that the portal vein contains two currents of venous blood, one coming from the superior mesenteric vein and going to the right lobe of the liver, the other from the splenic and inferior mesenteric veins passing into the left

lobe, so that abscesses and metastases of tumors would be located accordingly. In man there is definitely intermingling of blood so that too much reliance cannot be placed on this scheme.

Pyemic abscesses that are the result of appendiceal or intestinal infection may spread along intrahepatic vascular channels into the hepatic veins and from there by way of the inferior vena cava into the lungs and into the general circulation. In a recent clinical-pathological conference reported in the *New England Journal of Medicine* a case was described in which following a postappendiceal abscess, pulmonary and hepatic abscesses occurred. The discussant postulated that the cecal abscess must have led to septic thrombosis of the iliac vein and embolism from there into the lung, overlooking the fact that liver abscesses may readily spread into the lung following the natural venous drainage and that the introduction of an additional source of the septic pulmonary embolism was unnecessary. Surprisingly enough and anatomically without foundation, after the occurrence of the emboli in the lung and the diagnosis of the liver abscesses a ligation of the superficial femoral vein was done which of course was of no avail. Ligations of the tributaries of the portal vein, particularly of the ileocecal vein, in the presence of thrombosis, have been suggested in the literature, but modern chemotherapy is the method of choice.

In passing, the other modes of infection of the liver should be mentioned, since the liver is an ideal example for the multiplicity of sources of infectious spread. In addition to the portal vein, which is the main channel for the transmission of septic emboli, the hepatic artery is frequently responsible for the settling of infections in the liver, following infections of the general circulation such as osteomyelitis, endocarditis, carbuncles, respiratory infections, and pyemias from any source. A third source is direct ascending infection along the bile passages, also infections from the neighborhood such as paranephritic and perinephritic abscesses. Occasionally lymphatics from the appendix and gall bladder may transmit infections and finally a retrograde spread from the head by way of the superior vena cava, right heart, inferior vena cava, and hepatic veins has been reported.

Coming to the propagation of cancers to the liver we have the same organs of the gastrointestinal tract as sources of embolic spread and the same pathways, foremost among them the portal vein. Tumors concerned are, among others, cancers of the stomach, intestines including the rectum, and pancreas. There is an increasing tendency on the part of pathologists to regard cancerous spread by way of the blood stream as important as lymphatic propagation. Such an experienced observer as Miles who has pioneered the radical operation of rectal cancer, has been proved wrong when he stated that for practical purposes we can disregard the occurrence of portal spread to the liver. We know now how common bloodborne metastasis is in cancer of the rectum. Often several generations of metastases may be found in the liver, the first one being a localized metastasis brought to the liver by the portal vein, which secondarily has led to showers of daughter metastases around it (Willis).

It has been said that intravascular invasion, i.e., invasion of the portal territory occurs in $\frac{1}{5}$ of all cancers of the lower colon and rectum. The higher the grade of malignancy, the higher the incidence of venous involvement and the greater the chances of metastasis to the liver and from there to other organs. It seems that the vascular invasion is most apt to occur within the intestinal wall itself or within the perirectal tissue rather than at a distance. Thus early cancers may penetrate into the veins before they become locally inoperable (Glover and Waugh). The intravascular malignant thrombus encountered at necropsy or at operation is often found lying free within the lumen of the vessel, and the ease with which it can become detached is very apparent (Dukes and Bussey). This represents a warning against rough handling of the tumor and rectum before vessels are ligated

Evidence of tumorous growth within the hemorrhoidal veins is no absolute proof that the case is hopeless. But it is an indication that hematogenous spread is impending. Invasion of the veins with its danger of continuous or embolic spread of the malignant condition is an unpredictable event about

which very little can be done except resort to surgery at the earliest possible moment. It is the spread to the regional lymphatics that determines the scope and technique of the operation. The anatomical investigations of Miles on the lymphatic propagation of rectal cancer have determined the radical surgical approach in the same way as the anatomical studies of Halsted and Handley have done for cancer of the breast. The principles of lymphatic spread are the same in the two conditions. Phenomena such as the by-passing of lymph nodes by cancerous emboli or the reversal of the lymph stream in the presence of lymphatic obstruction with atypical involvement of nodes occur also in rectal cancer. The details of lymphatic drainage of the rectum and the mode of lymphatic spread of rectal cancer cannot be discussed here. But it is interesting to note that recently a reinvestigation of the lymph drainage of the highest portion of the rectum has been undertaken (Glover and Waugh). Based on the fact that the lymph stream from this part goes mainly upward along the superior hemorrhoidal vein, the proposition has been put forth to restrict the extent of rectal resection in cancer of the upper portion and to preserve the sphincteric apparatus. Without wanting to enter into a discussion of the merits of the problem, the anatomist is of course gratified to see that the pros and cons of the argument are offered on the basis of a study of the lymphatic anatomy of the region.

THE ANATOMICAL PRINCIPLES OF METASTATIC SPREAD

Having discussed some of the representative venous and lymphatic channels along which infections and tumors travel, it seems worthwhile to take up the subject of metastatic distribution from a more general angle and to dwell on the principles of tumor spread. Once a tumor has invaded the venous or lymphatic circulation, there exists the ever-present danger of tumor particles becoming dislodged. After this has taken place the tumorous emboli are a cellular component of the blood or lymph stream and as such are transported wherever the current leads them. Their flow will be arrested at a site that depends on the relative dimensions of vascular tube on the one hand and embolus on the other. Thus a metastatic embolus traveling in the general arterial stream reaches the smaller arterioles and is finally caught in the capillary network, if the embolus is of sufficient size, i.e., if it consists of more than a few cells. Somewhat more complex is the pathway through the liver. Two vascular channels, the portal vein and the hepatic artery, feed the capillary system of the liver and both are potential sources of metastatic emboli. Only one venous system, the hepatic veins, drains this organ. Still more intricate is the arrangement in the lung. Here the pulmonary artery transmits venous blood which, after oxygenation in the pulmonary capillaries, is collected in the pulmonary veins and brought to the left heart and from there into the general arterial circulation. In addition the bronchial arteries and veins form their own capillary network in the wall of the bronchi. The two systems anastomose freely. Most metastatic emboli are transported to the lungs by way of the pulmonary artery and are arrested in the capillary system of the lung. Here they may or may not take root. If they do, they may eventually break into the veins of the pulmonary or more rarely of the bronchial system. In the former case the emboli are transported into the general circulation, in the latter they are returned to the lungs by way of the azygos or innominate veins, superior vena cava, right heart, and pulmonary artery. Thus a new crop of pulmonary metastases may be set up as a result of this spread. Few emboli may also be brought to the lungs by way of the bronchial arteries from the general arterial circulation.

Figure 1 illustrates the capillary networks in a basic scheme of the circulation which has been developed by Walther: *a* is the capillary system of the lung; the upper part of the ellipse represents the arterial side, the lower part the venous side of the circulation. An embolus that enters the general circulation may be arrested in its capillary system (*c*) which is exemplified by the capillaries of the bone marrow, the brain, the skin, the kidney or any organ that drains directly into the caval system. In the case of a lung tumor that has invaded the pulmonary veins, the sys-

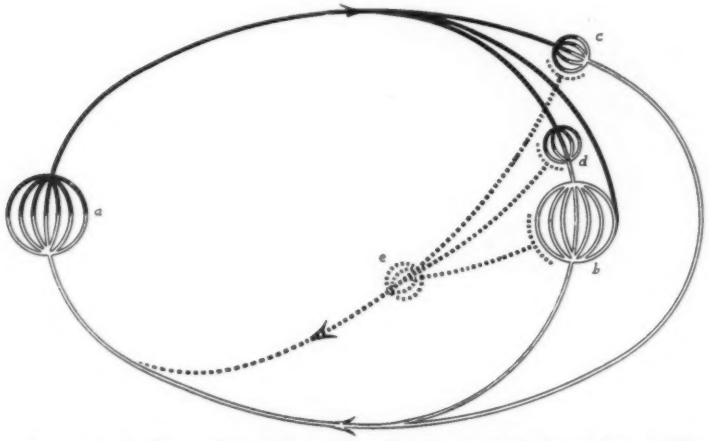


Fig. 1. Basic scheme of circulation. Heavy lines represent blood vessels containing arterial blood, double lines depict vessels containing venous blood, dotted lines lymphatics. *a*, Lung. *b*, Liver. *c*, Organs drained by venae cavae. *d*, Organs drained by portal vein. *e*, Regional lymph nodes. (Modified from Walther.)

temic capillary system is the first capillary filter which the embolus encounters. In contrast to this, an embolus that is dislodged from a cancerous thrombus in a peripheral vein is arrested in the capillary network of the lung (*a*). The systemic capillary network (*c*) then is the second filter for this tumor; *d* represents the capillary system of any organ that drains into the liver by way of the portal vein, such as the stomach, intestines, pancreas, and spleen; *b* is the portal capillary system of the liver. A tumor of the gastrointestinal tract that breaks into a vein, spreads to the liver and from there to the lung. The lung is therefore the second filter for this tumor and the peripheral capillary network the third. We also see that tumor emboli traveling in the general circulation may be brought directly to the liver by way of the hepatic artery. This is demonstrated by the arc to the right of *d*. We further notice in this diagram the lymphatic drainage represented as coming from *b*, *c*, and *d* terminating in the venous circulation by way of the thoracic duct; *e* represents the system of interposed regional lymph nodes. Thus a tumor arising in the gastrointestinal tract may by-pass the liver without metastasizing there and spread to the lungs via the lymphatics, the thoracic duct, superior vena cava, right heart, and pulmonary arteries.

According to this basic scheme there are then three or four types of metastatic spread (Walther): (1) The lung type whereby a tumor arising in the lung may break into the pulmonary vein and spread from there into the general arterial circulation (Fig. 2a). In this case the metastatic embolus could be arrested anywhere in the capillary bed of the periphery, be it the skin, the bone marrow, the kidney, the liver, or the brain. (2) The liver type (Fig. 2b). To this group belong the rare primary tumors of the liver for whom the first filter is the lung. (3) The vena cava type (the previous group is just a subheading of this group)(Fig. 3a) represented by all tumors that potentially break into and spread in the general venous circulation, i.e., most tumors, particularly those of the skin and its appendages—melanomas and breast cancers, tumors of the nervous system, nasopharynx, upper esophagus, lower rectum and anus, thyroid, bones, and urogenital system. (4) The portal type (Fig. 3b) in which a tumor metastasizes to the liver by way of the portal vein, then via hepatic veins, inferior vena cava, right heart, and pulmonary arteries to the lungs where a break-through into the pulmonary veins leads to spread into the general circulation. The shunt around the liver directly to the lung via the lymphatics likewise occurs.

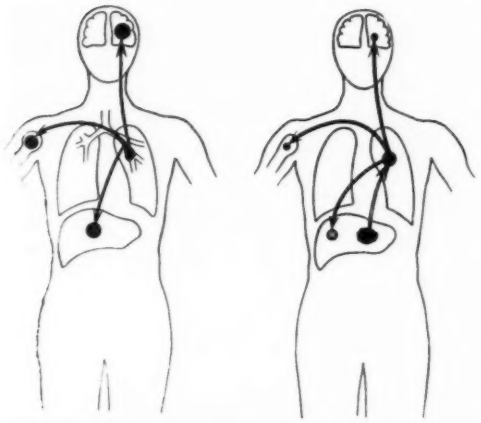


Fig. 2. Types of metastatic spread. a, left, Lung type. Tumor arising in the lung spreads, after invasion of pulmonary vein, into general arterial circulation, exemplified here by bone marrow, brain, and liver. b, Liver type. Primary tumor of liver spreads first to lung and from there as in a. (From Walther.)

To see this scheme in its proper perspective, one has to realize the importance and frequency of venous spread of cancer. According to Willis, it amounts to 50 per cent of all fatal cases. Once a metastasis has been set in any of the organs, it behaves like a primary tumor as far as the direction of its spread is concerned. It may easily break into a vein and set up a second generation of metastases. Thus different series of metastases may be superimposed and complicate the analysis (Willis).

An understanding of the pathways of lymphatic spread is somewhat complicated by the fact that once a lymph node is invaded, it may be blocked and a collateral lymph flow may be opened up with reversal of the lymph current and involvement of atypical nodes (Taylor and Nathanson). Atypical nodes may also become cancerous by a rather devious route, namely, as a result of lymphatic spread from an organ that has become secondarily involved by way of the blood stream. Conversely, metastatic cancer of the lymph nodes is apt to invade adjacent veins wherever these are in close proximity as e.g., in the neck, in the axilla, in the mediastinum, and in the pelvis.

Since we must assume from microscopic evidence at hand that many tumor emboli are considerably larger than the diameter of the capillaries we can postulate that such emboli are arrested in the first capillary network they encounter. Consequently it is not surprising that the commonest sites of metastatic involvement are the liver and lungs since for most tumors these organs represent the first and second capillary filters encountered.

Taking into account all anatomical facts listed we generally have no difficulty to explain the pathway which a certain metastasis has taken. The difficulty usually arises in accounting for the noninvolvement of certain organs. Thus the lung occasionally escapes in cancer that has metastasized into the general circulation. Particularly in cancer of the breast and prostate do we sometimes find an isolated metastasis in the body far away from the primary focus, yet without involvement of the lungs, a fact which is not compatible with our scheme. Many theories have been offered to explain the abnormal location of metastases (Willis). Only a few shall be discussed here. (a) Paradoxical or crossed embolism. An open foramen ovale is supposed to explain the passage of tumor emboli from the systemic veins

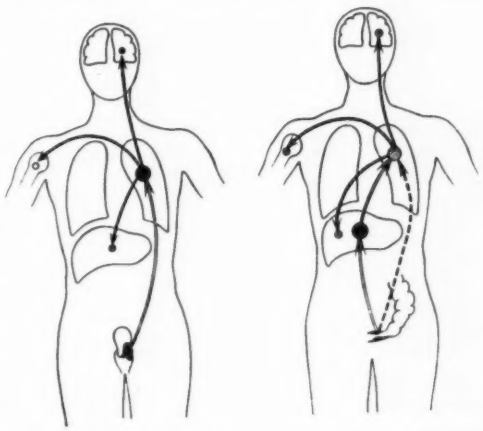


Fig. 3. Types of metastatic spread, continued. a, left, Vena cava type, represented by all tumors that invade the general venous circulation and exemplified here by tumor of the uterus. First filter is the lung. Spread from there by way of general arterial circulation as in 2 a. b, Portal type, represented by all tumors that invade portal circulation and exemplified here by tumor of the upper rectum. First filter is the liver, spread from there to lung, and then as in 2 a. Shunt around liver by way of lymphatics, thoracic duct, and venous circulation is shown by interrupted line. (From Walther.)

directly into the arterial circulation by-passing the lungs. This must be very rare since a functionally patent foramen ovale is a rather infrequent occurrence. (b) Retrograde venous embolism. Reversal of the blood flow in case of venous obstruction by a cancer may explain the presence of ovarian, vaginal, and epididymal metastasis in case of renal tumor. (c) The noninvolvement of the lungs in case of systemic metastasis has been explained on the basis of the passage of individual tumor cells through the pulmonary capillaries without arrest. While this may occur, probably the breaking off of clusters of tumor cells larger in diameter than the cross section of the pulmonary capillaries is more common. But it has to be realized that gross anatomical evidence of the absence of tumor tissue in the lungs does not prove noninvolvement of the lungs. In many cases careful microscopic search will reveal the presence of small emboli in the pulmonary arterioles.

THE VERTEBRAL VENOUS PLEXUS AND ITS SHARE IN THE SPREAD OF TUMORS AND INFECTIONS

In recent years, experimental and clinical proof has been offered for a pathway we were hardly aware of, but which removes many of the difficulties that are encountered in explaining the spread of metastasis and infection (Batson). As stated before, it is particularly the isolated involvement of the skeleton in metastatic spread of cancer of the breast and prostate which has baffled observers. How can metastatic emboli from the prostate reach the spinal column without being arrested in the lungs? In answer to this question, Batson called attention to a large venous system within and outside the spinal canal extending from the head to the sacrum, which had been described a century ago by the Frenchman, Breschet, and by German authors, but had since been forgotten (quoted from Harris). As these authors showed, there is a rich plexus of segmental veins on the outside of the spinal column anteriorly and posteriorly as well as inside the spinal canal. These veins also surround the spinal nerves within the intervertebral foramina and thus act as a cushion for the spinal nerves and the spinal cord. Another characteristic feature is the rich anastomoses of these veins, particularly in a longitudinal direction, but also the cross communications between right and left and from the inside of the canal to the outside. These veins are valveless and anastomose above with the cranial venous sinuses and below with the hypogastric veins.

In his experiments on human cadavers and later on live rhesus monkeys, Batson injected the dorsal vein of the penis with dyes and opaque media and found that the dye in addition to going to the inferior vena cava also entered the spinal veins and the vertebral plexus depending on the position of the body and on the viscosity and amount of material injected. After injection of 200 cubic centimeters of a thin mass the contrast medium did not fill the vena cava, but went along the vertebral veins to the skull. Repeated injections confirmed this and demonstrated filling of the venous sinuses of the cranial cavity. In the live monkey, after injection of thorotrast into the dorsal vein of the penis, filling of the caval system by way of the hypogastric and common iliac veins was noticed. Imitating the changed pressure conditions that take place in straining, coughing, sneezing, a towel was tied around the abdomen of the animal with the result that the contrast medium entered the vertebral veins. Injection into a venule of the breast of female cadavers led to extensive filling of vertebral veins and sinuses of the skull by way of the intercostal veins. The veins of the shoulder girdle and the vasa vasorum down to the elbow were likewise demonstrated.

Thus we have to regard the vertebral venous system as a plexus which contains a considerable amount of blood, more than is necessary for drainage of the organs it surrounds. It acts as a reservoir, a function which is facilitated by the absence of valves, by the rich anastomoses with other body veins and by its plexiform arrangement. We have to assume that the blood flow in this system is easily reversed following changing pressure conditions such as take place in straining. Batson's experiments demonstrate how freely the blood of the prostatic plexus and of the veins of the breast enters the vertebral plexus by-passing the systemic, pulmonary, and

portal circulation. This then is undoubtedly the pathway that is taken by cancerous emboli from the prostate to the pelvis and spinal column. It is in all probability also the channel used in the spread of carcinoma of the breast to the skeleton. Work by other investigators (Collis) has confirmed a path from the lung and pleura by way of the bronchial and intercostal veins and vertebral veins to the brain thus explaining the frequent occurrence of brain abscess in pulmonary infections and empyema, and metastasis to the skull and brain in pulmonary cancer. We now also understand the involvement of the cranial venous sinuses in puerperal fever which was mentioned in the beginning (Martin).

The recent investigations on the vertebral venous system have cleared up many of the difficulties in understanding the distribution pattern of cancerous and infectious emboli.

Having discussed the highways and byways along which metastatic spread takes place, one basic fact still needs to be pointed out: mechanical arrest of a tumor embolus is not identical with transformation of this embolus into a florid metastasis. Many emboli apparently never "take." We have to assume that tumor particles of sufficient size, once they have reached the general circulation, are deposited indiscriminately anywhere where the blood stream leads them and that their arrest is determined only by the relative size of the embolus and the capillaries it traverses. Why then, we must ask ourselves, are metastases so rare in certain locations such as skeletal muscles, the heart, spleen, the wall of the intestine, all of which have such a rich blood supply? And why is metastasis so common in other locations? Mechanical factors and reasons of vascular anatomy are insufficient to furnish an explanation although it has been attempted on this basis. Tissue susceptibility on one hand and general and local resistance on the other must be instrumental in determining the selection of metastatic sites. Experimental evidence on tissue cultures point to chemical factors such as oxygen tension, hydrogen-ion concentration, and the accessibility of growth-promoting hormones in the tissues as being responsible for the distribution of metastases (Willis). Recognizing that he has done his share once the roads of metastatic spread have been clarified, the anatomist leaves these problems to the biochemist and the cancer pathologist.

REFERENCES

1. Batson, O. V. Ann. Surg., 1940, 112: 138.
2. Idem. Ann. Int. M., 1942, 16: 38.
3. Braun, A. Sinus Thrombophlebitis. New York: Hoeber, 1928.
4. Case Record, Massachusetts General Hospital. N. England J. M., 1946, 234: 508.
5. Collis, J. L. J. Thorac. Surg., 1944, 13: 445.
6. Dukes, C. E., and Bussey, H. J. R. Proc. R. Soc. M., Lond., 1941, 34: 571.
7. Glover, R. P., and Waugh, J. M. Surg. Gyn. Obst., 1946, 82: 434.
8. Halsted, W. S. Ann. Surg., 1894, 20: 497.
9. Handley, W. S. Cancer of the Breast and its Treatment. 2nd ed. New York: Hoeber, 1922.
10. Harris, H. A. Brain, 1941, 64: 291.
11. Lachman, E. J. Oklahoma State M. Ass., 1944, 37: 153.
12. Martin, J. P. Brit. M. J., 1941, 2: 537.
13. Miles, W. E. Cancer of the Rectum. London: Harrison, 1926.
14. Ochsner, A., De Bakey, M., and Murray, S. Am. J. Surg., 1938, 40: 292.
15. Symonds, C. P. Brain, 1931, 54: 55.
16. Ibid., 1937, 60: 531.
17. Idem. Brit. M. J., 1940, 2: 348.
18. Taylor, G. W., and Nathanson, I. T. Lymph Node Metastases. London: Oxford University Press, 1942.
19. Walther, H. E. Zschr. Krebsforsch., 1937, 46: 313.
20. Willis, R. A. The Spread of Tumors in the Human Body. London: Churchill, 1934.

CHOLECYSTITIS AND CHOLELITHIASIS

An Analytical Report of 1,104 Operative Cases

RALPH ADAMS, M.D., and ALLAN STRANAHAN, M.D., Boston, Massachusetts

THIS report is a comprehensive review of 1,104 cases in which a diagnosis was made of stone in the gall bladder or bile ducts and operation was carried out at the Lahey Clinic during a 4 year period which ended December 31, 1945.

ETIOLOGY

There are few new facts to report regarding the etiology of gallstones. Recent work by Womack and Hoffner indicates that cholesterol in the wall of the gall bladder is another etiologic factor in addition to stasis, infection, and metabolic disturbance. Most of our patients were obese, but it is interesting to note that 1 patient had concurrent cholelithiasis and mild primary hyperthyroidism.

INCIDENCE

Of the 1,104 patients 831 (75.2 per cent) were between 31 and 60 years of age. The youngest was 9 and the eldest 81 years. Hamilton and associates reported a case of cholelithiasis in a child of 8 and Potter a case in a child of 4½ years.

It is generally recognized that gallstones occur more frequently in women than in men. In this series there were 838 females (76 per cent) and 266 males (24 per cent), a ratio of 3 to 1.

The increased incidence of gallstones in the obese likewise is common knowledge. A large percentage of these patients were overweight; however, the chief complaint of many patients, other than their abdominal distress, was weight loss. This was noticed most frequently in the group with common duct stones. Weight loss also occurred in certain patients without common duct stones who had had frequent attacks of biliary colic. This is probably explained on the basis that the patients restricted the diet because of their fear of distress following the intake of food.

From the Department of Surgery, The Lahey Clinic.

SYMPTOMS AND SIGNS

Pain was the predominant symptom, being present in 93.2 per cent of the cases. It was usually localized in the right upper quadrant of the abdomen and was typical biliary colic extending to the right scapula. In many cases the pain was severe and constant rather than of a colicky nature. Following these attacks, there was usually residual tenderness over the region of the gall bladder. Complaints of vague abdominal distress, and occasionally of pain in the left upper quadrant or lower abdomen, were encountered more frequently than was anticipated.

One patient with cholelithiasis and choledocholithiasis without jaundice had no pain. One patient who suffered from pain was found at operation to have fibrosis of the cystic duct without cholelithiasis. Two patients had painless jaundice with cholelithiasis and common duct stones.

Nausea, vomiting, and dyspepsia were the next most prevalent symptoms (64.9 per cent). Those patients with nausea and vomiting always had dyspepsia, but many had dyspepsia without nausea and vomiting. Dyspepsia without other symptoms was present in 20 cases (1.8 per cent). In 26 cases (2.3 per cent) there were no symptoms. Many of these were cases in which gallstones were discovered during routine abdominal exploration at operations done for other conditions.

Fever was present in many cases of acute and subacute cholecystitis and of obstruction of the bile duct. No relevance was detected, however, in its relationship to common duct stones either with or without jaundice.

JAUNDICE

Two hundred patients (18.1 per cent) gave a previous history of jaundice or had jaundice when seen at the clinic. Jaundice was present in 95 (51 per cent) of the 186 cases in which common duct stones were removed, and in 105

(52.5 per cent) of the 200 jaundiced cases, common duct stones were not found at operation. One hundred eighty-six cases had proved common duct stones but almost one-half (89 or 47.8 per cent) of these patients with common duct stones did not have jaundice. Painless jaundice occurred in 2 patients with common duct stones.

From these figures it appears that jaundice indicates common duct stones in only 50 per cent of the cases. In the other 50 per cent, the jaundice was the result of an associated hepatitis or cholangitis. The presence or absence of jaundice is an important but a treacherous sign. Fifty per cent of patients who have common duct stones do not have jaundice and in only 50 per cent of patients with jaundice have common duct stones been discovered.

The *physical findings* depended usually on the extent of the pathologic process. There was considerable spasm and rigidity over the right upper part of the abdomen in acute disease of the gall bladder. In a few instances a diagnosis of acute cholecystitis was made on the basis of physical findings and chronic gall-bladder disease was found at operation; and vice versa, empyema of the gall bladder has been found when chronic cholelithiasis was expected.

ROENTGENOLOGIC EXAMINATION

Either oral or intravenous cholecystographic examination of the gall bladder was made in 910 of the 1,104 cases (82.4 per cent). One hundred ninety-four patients had no roentgenologic examination. The cases not examined included those in which gallstones were an incidental finding, many who had secondary biliary tract operations, and some with jaundice in which it was not thought of value to give the dye.

A correct diagnosis was made in 888 of the 910 patients (97.6 per cent) examined roentgenologically. In 559 cases (61.4 per cent) stones were visualized either with or without the gall-bladder dye. In 197 cases (21.6 per cent) a diagnosis of nonfunctioning gall bladder was made, and in all of these cases, stones were found at operation. In 25 cases (2.7 per cent) a diagnosis of nonfunctioning gall bladder was made and no stones were found at laparotomy, but 19 of these cases had microscopically proved chronic cholecystitis. Many of these were of the cholesterosis or "strawberry" group. The roentgenologic diagnosis of common duct stone was made and proved at operation in only 2 cases.

Right-sided renal calculi plus gallstones occurred in 2 patients and the renal stones were later proved to be present by retrograde pyelograms. A diagnosis of situs transversus was made in 2 cases and cholecystectomy was done through a left upper rectus incision. Pancreatic lithiasis was suspected once, and proved by subsequent operation.

A diagnosis of irritable bowel or functional indigestion associated with gall-bladder disease was made in 132 patients (12 per cent) of the total number of the 1,104 patients. These patients were all treated before and after the gall-bladder operation for this condition.

Roentgenologic studies were misleading or erroneous in 22 (2.4 per cent) of the 910 patients examined. Twelve patients had normal cholecystograms, 5 of these had stones at operation, and the remaining 7 had chronic cholecystitis. In 8 cases the cholecystogram was interpreted as showing cholelithiasis, but no stones were found at operation. A diagnosis of nonfunctioning gall bladder was made in 1 case in which a normal gall bladder was found at laparotomy. An x-ray diagnosis of papilloma of the gall bladder was made in 1 case, but not found at operation.

Because of the generally poor results from cholecystectomy for noncalculous cholecystitis, before a surgical procedure is proposed in cases of faulty visualization of the gall bladder without demonstrable stones, certain criteria must be met (34, 49): (1) all other likely causes for the symptoms have been eliminated; (2) there is sufficient pain to warrant an attempt at relief by cholecystectomy; (3) a cholecystogram is abnormal on at least two tests.

Medical treatment of suspected or confirmed coexisting digestive disturbances has failed to relieve the symptoms.

PREVIOUS SURGERY

One hundred fourteen patients (10.3 per cent) had had previous biliary tract surgery.

Forty-eight patients had cholecystostomy (3 of these had two cholecystostomies), 38 had cholecystectomy and 15 had cholecystectomy and choledochostomy.

SURGICAL AND PATHOLOGIC FINDINGS

Normal gall bladder. Cholecystectomy was done in 6 cases in which the pathologic report was normal gall bladder. One patient had a nonfunctioning gall bladder by cholecystographic examination associated with hepatitis and jaundice. In 2 cases a diagnosis of stones was made from roentgenograms, including both a scout film and a cholecystogram; in 1 of these, the calcification was found to be in the liver. Three patients were operated on because of severe pain which was not controlled by medical management and thought to be caused by biliary tract disease. In 1 of these cases a cholecystogram was taken and the gall bladder was normal. In the other 2, no roentgenograms of the gall bladder were taken, in one of these jejunitis was found which explained the symptoms and in the other no abnormality was found. None of 6 specimens determined from microscopic study to be a normal gall bladder contained stones.

ACUTE GALL-BLADDER DISEASE

The treatment of acute cholecystitis is a problem about which there still is not full agreement. Nearly everyone (4, 18-20, 26, 31, 48, 52) agrees that early surgery (that is, within 24 to 72 hours after onset) after adequate preoperative preparation, is the best policy. There remain occasional clinicians (3) who feel that the danger of gangrene and perforation is overstressed; there are still others (18) who do a cholecystostomy more frequently than a cholecystectomy for acute cholecystitis. It has been our policy (31, 39) for several years to treat patients with acute gall-bladder disease as an abdominal emergency demanding immediate hospitalization, restoration of fluids, replenishment of the glycogen reserve, correction of altered blood chemistry, and early operation. Cholecystectomy is unquestionably the operation of choice, gall-bladder drainage being used only in the case of very ill patients who present other complicating factors.

Fifty-five patients (5 per cent) were seen with acute gall-bladder disease. Fifty-one (92.7 per cent) of these 55 cases had cholelithiasis. The common duct was explored in 10 cases and stones were found in 6 of these cases. The relationship of jaundice to common duct stones was about the same in acute disease as in chronic disease of the gall bladder. Pericholecystic disease (abscess and fistula) was found in 9 of the patients with acute disease of the gall bladder. There were no free perforations. Two deaths occurred in this small series, a mortality rate of 3.6 per cent.

CHRONIC DISEASE OF THE GALL BLADDER

It is the policy at the clinic to advise cholecystectomy in all cases of gallstones, as we feel that the morbidity and mortality rates are less from the operation than from the possible complications of calculi of the biliary tract. We feel that the so-called "silent gallstone" is a rare occurrence; if a careful history is elicited, some symptoms are obtained. Although there were 26 patients in this series with no symptoms recorded, we found that a careful history was not taken in these cases. Most of these patients came with other presenting complaints and the gallstones were an incidental finding.

Chronic cholecystitis with cholelithiasis was by far the most common finding—789 cases. There were 51 cases of chronic cholecystitis, 159 cases of cholelithiasis and common duct stones, and 2 of chronic cholecystitis and common duct stones. Gallstones were found in 13 patients who were operated on for other conditions, such as pelvic tumors, and carcinoma of the colon.

Cholecystitis is frequently associated with other conditions. Peptic ulcer was the most common, occurring in 61 cases. The diagnosis in nearly all instances was established by roentgenologic study of the gastrointestinal tract before operation. Fifty-nine of these were duodenal ulcers. All the patients with peptic ulcer were treated medically after operation.

Diaphragmatic hernia was the next most common associated condition (12 cases). Although the two conditions were at times difficult to distinguish, usually a cholecystec-

tomy was done and in only 2 of the cases was it found necessary to repair the hernia.

Cholelithiasis was also found in conjunction with ulcerative colitis, regional ileitis, sigmoidal divericulitis, and rheumatoid arthritis. A cholecystectomy was done in an attempt to relieve the symptoms in these conditions.

No attempt was made in this series to tabulate the correlation between heart disease and cholelithiasis. Hurxthal and Dolgin have recently reviewed 559 cases of proved cholecystitis and cholelithiasis, and found that 53 patients (9.5 per cent) had associated heart disease. Their impression is that the incidence of heart disease is not any higher in patients with gall-bladder disease than it is in any other group of patients of the same age or sex distribution. They state that cholelithiasis may be responsible for varied electrocardiographic changes, but they do not believe that cholecystectomy will have any effect on the heart disease itself other than to eliminate the electrocardiographic findings caused by the cholelithiasis. Distinction between acute gall-bladder disease and heart disease is at times difficult but usually by careful study the differential diagnosis can be made.

TUMORS OF THE GALL BLADDER

Tumors of the gall bladder are not common. Only 4 tumors were found in 1,036 cholecystectomies, as follows: 1 benign papilloma, 1 malignant adenoma, and 2 adenocarcinomas. The incidence of carcinoma in this series is only 0.3 per cent. This is much lower than in a previously reported series (41), and a series by Vadheim, Gray, and Dockerty. In 3 of the 4 cases a diagnosis of cholelithiasis was made from the roentgenogram and the fourth patient, who had a benign papilloma was operated on for acute cholecystitis. All 4 of these patients were operated on and all had gallstones. The incidence of gallstones with carcinoma in this series was 100 per cent, while others (5, 22, 29, 36, 37, 42) report an incidence of 76 to 87 per cent. When the diagnosis is made preoperatively, the lesion is usually too extensive for any chance of cure. Cases correctly diagnosed preoperatively as carcinoma of the gall bladder are not included in this report.

COMMON AND HEPATIC DUCT STONES

The philosophy of our surgical staff in regard to exploration of the common bile duct has been stated and restated (8, 9, 12, 30, 35). The present study corroborates our previous experiences (9) that there is no certain way to tell whether or not common duct stones are present. Suggestive points are often found in the history, physical examination, and at operation which lead one to believe that common duct stones are present or absent. Neither the mortality nor the morbidity is appreciably increased with common duct exploration, especially with the anesthesia (43) and preoperative preparation (1) employed at the present time. We believe, therefore, that the common duct should be explored for any of the following indications: (1) frequent acute attacks of biliary colic, chills, or fever; (2) past or present history of obstructive jaundice or laboratory signs thereof; (3) dilated or thickened common duct; (4) multiple small stones in the gall bladder; (5) unsatisfactory or suspicious findings on palpation; (6) sediment in aspirated bile from the common duct; (7) noncalculous gall bladder with biliary tract symptoms; (8) small contracted gall bladder; (9) acute or subacute pancreatitis or hepatitis.

The common duct was explored in 504 cases (45.7 per cent) and stones were found in 186 cases (16.8 per cent); 36.9 per cent of the ducts explored contained stones. There were 161 cases of cholelithiasis and common duct stones, 17 cases of common duct stones after previous cholecystectomy (done elsewhere), and 4 each of common duct stones with cystic duct remnant and with fibrosis of the sphincter of Oddi.

Occasionally one will find a dilated common duct and ampulla associated with cholelithiasis but no common duct stones. In these cases there usually are other indications for choledochostomy besides dilatation of the duct. We believe the recent passage of a common duct stone is frequently the explanation of such a finding. Also, patients may give a typical history of recurrent common duct stones and exploration will yield negative results. This occurred 6 times in this series.

Foreign bodies in addition to stones in the common duct are rare. Manson-Bahr and

Walton reported the removal of a liver fluke from the common duct and Crawford reported an autopsy in which the blade of a hemostat was found in the common duct 7 years after a cholecystectomy. Removal of a broken T-tube relieved recurrent obstruction of the common duct in 1 case in this series.

PANCREATITIS AND BILIARY TRACT DISEASE

Pancreatitis was found to be associated with biliary tract disease in 26 cases (2.35 per cent). The etiology of pancreatitis is quite generally considered to be the reflux of bile or pancreatic juice into the pancreatic duct caused either by a stone impacted in the ampulla of Vater or by anatomical variations in which both the duct of Wirsung and common bile duct open into the ampulla (47). In this type of relationship any spasm of the sphincter of Oddi may cause a diversion of the biliary flow. Also, in certain instances there may be a hyperplasia of the epithelium of the pancreatic duct with an obstruction to the flow of pancreatic fluid, resulting in varying degrees of pancreatitis (47).

It has been our experience in the past (8, 22, 31) that direct surgery on the pancreas itself is rarely indicated. We do not believe that it is wise to incise or drain the pancreas. We consider pancreatitis to be a complication of disease of the biliary tract and, therefore, we usually drain the common bile duct and remove the gall bladder if indicated (33).

A diagnosis of interstitial pancreatitis or chronic pancreatitis is rarely made preoperatively and when found, is merely more evidence for choledochostomy. Patients with acute hemorrhagic pancreatitis are rarely operated upon in the acute stage as early surgery in these cases carries a very high mortality risk. When acute cholecystitis occurs in conjunction with acute interstitial pancreatitis, the diagnosis may be difficult and delay in surgery may be fatal.

In this series pancreatitis was found with cholelithiasis and a normal common duct in 8 cases, and with chronic cholecystitis and a normal common duct in 5 cases. Chronic pancreatitis was found together with stricture of the common duct in 1 case, similar to those cases reported by Peterson and Cole.

INTERNAL BILIARY FISTULA

An internal biliary fistula occurs more commonly than is generally thought. There were 16 cases in this series. They may be classified into two groups, as spontaneous, and as those caused by a previous surgical procedure.

Spontaneous biliary fistula has been adequately reported by others (17, 50). This condition is rarely considered as a preoperative diagnosis, unless there has been a history of passage of gallstones by rectum, or an intestinal obstruction caused by an impacted gallstone (40). Also, a severe attack of biliary colic is sometimes followed by a period during which the patient is free of symptoms. This sequence is suggestive of a spontaneous fistula, especially if the patient has a long preceding history of disease of the biliary tract. If there is air in the biliary tree or if barium is seen in the biliary system during gastrointestinal examination, this is presumptive evidence of an internal fistula.

A previous surgical procedure was the cause of a biliary fistula in 4 of our cases. Two patients had had a cholecystjejunostomy and two others a choledochoduodenostomy.

Ten of the patients with a spontaneous fistula had connections between the gall bladder and duodenum, 1 between the gall bladder and colon, and 1 between the gall bladder and common duct.

It is advisable to close the fistula at the time of cholecystectomy; otherwise complications may arise, such as ascending cholangitis, which occurred in 2 cases in this series.

BENIGN STRICTURES OF THE BILE DUCT

Benign strictures of the bile duct comprise but a small group (23 cases) in this series and are mentioned only because a diagnosis was made of associated biliary calculi. In many of these cases a diagnosis was made of recurrent or residual stones of the common duct. This number is but a small percentage of the strictures that have been seen at the Lahey Clinic during the past few years. As of December 31, 1945, 176 patients had been referred here and operated upon for stricture of the common bile duct (6).

The causes and methods of repair used have been presented by Cattell (10); however, it

might be well to review them briefly at this time. The causes are: (1) ulceration from gallstones; (2) inflammation of common bile duct; (3) operative injuries, (a) excision of portion of duct, (b) clamping during operative hemorrhage; (4) following subtotal gastrectomy; (5) chronic sclerosing pancreatitis.

By far the most common cause of stricture is operative injury which comprises over 80 per cent of the cases.

The prevention of benign strictures, as far as operative injury is concerned, is based mainly on adequate exposure (32) so that a careful anatomical dissection can be carried out. Lahey has mentioned this fact many times (30-33, 35).

The diagnosis of stricture is often difficult to make; it is frequently confused with common duct stones or carcinoma of the bile duct or pancreas. If after a cholecystectomy jaundice develops immediately (in 1 to 3 weeks) or if the fistula at the site of the T-tube drains over a long period of time and if, in addition, there is a history of operative injury or hemorrhage, a stricture probably is present. Patients with stricture gradually become jaundiced following the closure of the external biliary fistula, and usually remain so until another operation is done, or an internal fistula develops in the interim.

Twenty-three strictures of the bile duct were encountered in this series: 4 had been caused by operative injury, 1 by cholangitis, 17 by fibrosis of the sphincter of Oddi, and 1 by fibrosis of the cystic duct and chronic cholecystitis.

Fibrosis of the sphincter of Oddi is not an uncommon condition; it was found in 17 cases in this small series. It occurs usually following previous bile duct surgery in which the sphincter may have been dilated too vigorously. As proof that this is not always the cause, however, it was present in 2 cases in which the patients had not had previous surgery and only 1 of these patients had common duct stones.

POSTCHOLECYSTECTOMY SYNDROME

The causes of symptoms following cholecystectomy with or without choledochostomy are many. Various aspects of this subject have been discussed by numerous authors (7, 11, 13, 14, 16, 21, 24, 25, 28, 44, 53, 54). The different causes as they were found in this series are briefly outlined: (1) benign stricture of common duct; (2) residual pancreatitis or hepatic disease; (3) common duct stones; (4) irritable bowel or functional indigestion (132 cases); (5) gall-bladder or cystic duct remnant (12 cases); (6) biliary dyskinesia and spastic sphincter of Oddi (7 cases); (7) adhesions of duodenum to gall-bladder fossa (8 cases); (8) duodenal diverticulum simulating gall-bladder colic.

The first three causes have been discussed elsewhere in this paper.

Irritable colon or functional indigestion was present in 12 per cent of the cases. A diagnosis of this condition was usually made preoperatively and medical therapy instituted. According to Ivy and Goldman, constipation may cause stimulation of various splanchnic nerves and predispose to stasis of the biliary tract by decreasing bile formation, and by increasing the resistance to the flow of bile through the sphincter of Oddi into the duodenum. Wilkinson stated that symptoms of irritable colon are just as varied as those of cholecystitis. There may be epigastric distress, belching, distention, shifting abdominal pain, and nausea and vomiting. Recognition and treatment of this condition will decrease the incidence of poor results after cholecystectomy, particularly in that group of patients who complain of dyspepsia alone.

A remnant of the gall bladder or cystic duct has been recognized for several years (12, 21) as a possible cause of distress after cholecystectomy. We believe that, with adequate exposure and anatomical dissection, such a surgical error can always be avoided. In this series there were 12 cases, 7 with stone in the remnant and no common duct stones, 4 cases with a remnant without stone and choledocholithiasis, and 1 case in which stones were found in the remnant and the common duct was not explored. One should be able to achieve a good result by removing the cystic duct remnant if the first operation were clearly indicated (21).

We consider biliary dyskinesia and spastic sphincter of Oddi in the same category. The

cause of this condition is not definitely known. Mild symptoms of dyskinesia are undoubtedly more frequent than our few cases would indicate. The only patients who were operated on in this group were those who did not respond to strict medical management. There were 7 patients, 2 with jaundice without common duct stones and 5 with no jaundice and no common duct stones.

Adhesions of the duodenum to the gall-bladder fossa following cholecystectomy constitute a condition about which very little is written. This condition is very common, but rarely causes severe symptoms. It is usually recognized only at operation, the symptoms having been thought to be caused by common duct stone or stricture. The duodenum is firmly adherent and usually rotated so it may partially obstruct both the duodenum and the common duct. There were 8 cases in this series in which symptoms occurred. All 8 patients had pain in the right upper quadrant, either intermittently or constantly, all had occasional nausea and vomiting and there was a history of jaundice in 2 of the cases. All were relieved by release of the adherent duodenum and by placing the omentum in the fossa so that the adhesions would not recur.

In order to prevent this complication, one should carefully reperitonealize the gall-bladder fossa and common duct and then place a small portion of the omentum in this region between the liver and duodenum.

Duodenal diverticula are usually symptomless. They were found to be associated with biliary tract disease in 9 cases. It is not believed necessary to resect them unless they have a very narrow neck. Resection was done only once (together with cholecystectomy) in this series. In 1 case which has already been reported (24) the diverticulum was not found until the fourth abdominal operation. This diverticulum contained gallstones and had a narrow neck. Resection of the diverticulum gave complete relief.

SURGICAL PROCEDURES

Cholecystostomy was done in only very ill patients who had some other complicating disease. Drainage of the gall bladder was done in 6 cases (0.54 per cent) and all were for acute cholecystitis. This incidence is much lower than any other reported series of cases known to us.

Cholecystectomy alone was done in 582 cases. Cholecystectomy with choledochostomy was done in 454 cases.

There were 114 patients who had secondary surgery of the biliary tract. Three patients had operation directed toward the treatment of peptic ulcer along with cholecystectomy: 1 a gastric resection, and 2 had gastroenterostomy.

In 9 cases cholecystectomy was performed for acute cholecystitis occurring during the immediate postoperative course of some other condition: 3 after abdominoperineal resection, 2 after thyroidectomy, 2 after transthoracic resection of the esophagus, 1 each after a pelvic laparotomy and a transurethral resection.

Appendectomy was performed in conjunction with the biliary tract surgery in 400 cases. We do not believe that appendectomy increases the mortality or morbidity. During the pathologic examination in one of the appendectomy cases, a carcinoid of the appendix was discovered.

POSTOPERATIVE COMPLICATIONS

Seventy-two of the 1,104 patients (6.5 per cent) had postoperative complications.

Stricture of the bile duct thought to have been caused by operative injury occurred in 1 case. Inflammatory stricture occurred in 1 case. This patient had a small but grossly thickened and acutely inflamed common duct at the time of initial operation, when stones were removed from the duct and a contracted gangrenous gall bladder was removed. A tiny T-tube was inserted, but this became plugged and had to be withdrawn. In the course of the next 3 months fibrous stenosis of the middle third of the common duct developed through which a 1 millimeter lumen persisted. At a second operation, the stenotic portion was resected and the ends anastomosed over a vitallium tube.

Atelectasis or pneumonia or both was a complication in 10 patients (0.9 per cent).

Phlebitis or phlebothrombosis developed during the immediate postoperative period in 16 patients (1.45 per cent). Eight patients

had pulmonary emboli, 2 fatal and 6 nonfatal. One pulmonary embolus occurred shortly after a varicose vein ligation and retrograde injection 13 days after the cholecystectomy. None of the patients with pulmonary emboli had clinically detected evidence of phlebitis.

Major wound infection occurred in 7 patients; 3 of these had cholecystectomy and appendectomy; 1 had appendectomy and choledochostomy, and 3 had simple cholecystectomy. The abdominal drains emerged through the primary incision in all of these cases.

Right subdiaphragmatic abscess occurred in 1 case and there was 1 left subdiaphragmatic abscess in a case of situs transversus in which a pseudodiverticulum of the transverse colon was excised in addition to cholecystectomy. There was 1 patient who had a right subhepatic and right subdiaphragmatic abscess; appendectomy and cholecystectomy were done in this case.

Two patients had wound dehiscence; 1 of these had cholecystectomy, appendectomy, and choledochostomy with choledocholithiasis.

Hernia in the scar occurred in 16 cases (1.45 per cent). One patient had associated wound infection, 5 had cholecystectomy and appendectomy, 1 had cholecystectomy and choledochostomy without common duct stones, and 1 had secondary biliary tract surgery.

Bacillus welchii peritonitis occurred in 1 patient and was fatal. This rare complication has been reported before (2). There have been only 3 cases in 5,000 operations on the biliary tract. It is thought to be caused by reflux of infected duodenal contents into the common duct after dilatation and irrigation of the common duct with isotonic solution of sodium chloride. We now advise that the catheter used be kept in the common duct and not be passed through to the duodenum, and only moderate dilatation of the sphincter be done.

There were 2 patients who had an exacerbation of gout during their postoperative convalescence. Two had parotitis.

One patient had a massive gastric hemorrhage on his fourteenth postoperative day and a posterior gastroenterostomy was done. He now has symptoms of a jejunal ulcer.

MORTALITY RATE AND ANALYSIS OF DEATHS

There were 1,104 operations, 10 deaths, making a mortality rate of 0.9 per cent.

Analysis of deaths. One death occurred in a women 62 years old who had cholelithiasis, choledocholithiasis, and a diaphragmatic hernia which was repaired at the time of the cholecystectomy and choledochostomy. She died on the twelfth postoperative day. Autopsy showed Bacillus welchii peritonitis, pancreatitis, and cerebral thrombosis.

Death occurred in a 28 year old man with cholelithiasis in whom cardiac arrest took place after a spinal anesthesia. He died on the fifteenth postoperative day of pneumonia and lung abscess.

A third death was in a 65 year old woman who had cholelithiasis, choledocholithiasis, and duodenal ulcer. She had a cholecystectomy, choledochostomy, and subtotal gastric resection. Death occurred on the fourth postoperative day of bronchopneumonia.

A fourth death was in a 63 year old man who had acute cholecystitis with common duct stone. While getting out of bed 12 days after cholecystectomy and choledochostomy he had a massive pulmonary embolus.

The fifth death was in a 55 year old man with interstitial pancreatitis and cholelithiasis. He died on the eleventh postoperative day after cholecystectomy and choledochostomy of massive pulmonary embolus, confirmed by autopsy.

The sixth death occurred in a 50 year old man with cholelithiasis; he had a hemoptysis 36 hours postoperatively which was thought to be caused by a pulmonary embolus. He died shortly thereafter and autopsy showed massive lobar atelectasis secondary to a large mucous plug in a primary bronchus.

A 65 year old woman with cholelithiasis had a cholecystectomy and died on the seventh postoperative day of coronary occlusion, the diagnosis being corroborated by an electrocardiogram.

A 74 year old man with acute cholecystitis died 24 hours after cholecystectomy. Autopsy was not performed; death was thought to be caused by "liver failure."

A 50 year old woman with a cystic duct remnant, chronic pancreatitis and hepatitis

died 24 hours after excision of the cystic duct remnant and a choledochostomy. No autopsy was obtained; death was thought to be caused by "liver failure."

A 57 year old man had had 3 previous operations and was in very poor condition from a gastropancreaticoduodenal cutaneous fistula. He died on the thirteenth postoperative day after cholecystectomy, choledochostomy, closure of a gastric fistula, and drainage of a pancreatic fistula and cyst. There was a large mass in the head of the pancreas. Curettage of the base of the pancreatic tumor showed mucinous carcinoma of pancreas. No autopsy was obtained.

REFERENCES

1. Adams, R. Surg. Clin. N. America, 1943, 23: 673-677.
2. Ibid., 1944, 24: 551-553.
3. Bachhuber, C. A., Deeb, P. H., and Taylor, E. A. Am. J. Surg., 1945, 67: 40-47.
4. Berk, J. E. Am. J. Digest. Dis., 1940, 7: 325-332.
5. Burrows, H. Brit. J. Surg., 1939, 27: 166-168.
6. Cattell, R. B. Personal communication to the authors.
7. Idem. Ann. Surg., 1929, 89: 930-941.
8. Idem. Surg. Clin. N. America, 1943, 23: 644-646.
9. Ibid., 694-700.
10. Ibid., 701-713.
11. Cattell, R. B., and Kiefer, E. D. J. Am. M. Ass., 1929, 93: 1270-1273.
12. Clute, H. M., and Swinton, N. W. Surg. Gyn. Obst., 1934, 59: 906-912.
13. Cole, W. H. J. Michigan M. Soc., 1940, 39: 173-179.
14. Colp, R. Bull. N. York Acad. M., 1944, 20: 203-219.
15. Crawford, B. L., and Stewart, H. L. Am. J. Clin. Path., 1939, 9: 353-360.
16. Doehring, P. C. Arch. Surg., 1941, 42: 665-680.
17. Eliason, E. L., and Stevens, L. W. Am. J. Surg., 1941, 51: 387-392.
18. Idem. Surg. Gyn. Obst., 1944, 78: 98-103.
19. Fallis, L. S., and McClure, R. D. Surg. Gyn. Obst., 1940, 70: 1022-1028.
20. Glenn, F. Surg. Gyn. Obst., 1939, 69: 431-435.
21. Gray, H. K., and Sharpe, W. S. Proc. Mayo Clin., 1944, 19: 164-168.
22. Greenwald, W. Surgery, 1944, 16: 370-376.
23. Hamilton, H. B., Rich, C. O., and Bisgard, J. O. J. Am. M. Ass., 1934, 103: 829-830.
24. Hare, H. F., and Cattell, R. B. Surg. Clin. N. America, 1944, 24: 635-639.
25. Hill, H. A. Radiology, 1937, 29: 261-278.
26. Hotz, R. Am. J. Surg., 1939, 44: 706-711.
27. Hurxthal, L. M., and Dolgin, M. D. Personal communication to authors.
28. Ivy, A. D., and Goldman, L. J. Am. M. Ass., 1939, 113: 2413-2417.
29. Kirshbaum, J. D., and Kozoll, D. D. Surg. Gyn. Obst., 1941, 73: 740-754.
30. Lahey, F. H. Am. J. Surg., 1938, 40: 209-216.
31. Idem. Surg. Clin. N. America, 1940, 20: 793-801.
32. Idem. Surg. Gyn. Obst., 1942, 75: 445-448.
33. Idem. Surg. Clin. N. America, 1943, 23: 639-643.
34. Lahey, F. H., and Jordan, S. M. Am. J. Surg., 1931, 11: 1-5.
35. Lahey, F. H., and Swinton, N. W. N. England J. M., 1935, 213: 1275-1280.
36. Lichtenstein, G. M., and Tannenbaum, W. Ann. Surg., 1940, 111: 411-415.
37. Liebowitz, H. R. Am. J. Digest. Dis., 1939, 6: 381-387.
38. Manson-Bahr, R., and Walton, J. Brit. J. Surg., 1941, 28: 380-383.
39. Marshall, S. F. Surg. Clin. N. America, 1943, 23: 647-653.
40. Marshall, S. F., and Mitchell, B. D. Surg. Clin. N. America, 1944, 24: 648-655.
41. Marshall, S. F., and Morgan, E. S. Surg. Clin. N. America, 1938, 18: 687-693.
42. Mattson, H. Minnesota M., 1942, 25: 985-988.
43. Nicholson, M. J. Surg. Clin. N. America, 1943, 23: 678-693.
44. O'Donnell, L. D. Pennsylvania M. J., 1939, 42: 1315-1319.
45. Peterson, L. W., and Cole, W. H. Arch. Surg., 1945, 51: 15-21.
46. Potter, A. H. Surg. Gyn. Obst., 1928, 46: 795-808.
47. Rienhoff, W. R., and Pickrell, K. L. Arch. Surg., 1945, 51: 205-219.
48. Smith, B. C. Surg. Clin. N. America, 1945, 25: 285-300.
49. Tracey, M. L. Surg. Clin. N. America, 1943, 23: 669-672.
50. Tracey, M. L., and McKell, D. M. Jr. Surg. Clin. N. America, 1943, 23: 717-727.
51. Vadheim, J. L., Gray, H. K., and Dockerty, M. B. Am. J. Surg., 1944, 63: 173-180.
52. Wallace, R. H., and Allen, A. W. Arch. Surg., 1941, 43: 762-772.
53. Weir, J. F., and Snell, A. M. J. Am. M. Ass., 1935, 105: 1093-1098.
54. Wilkinson, S. A. J. Am. M. Ass., 1937, 109: 1012-1014.
55. Womack, N. A., and Hoffner, H. Ann. Surg., 1944, 119: 391-410.

A STANDARDIZED METHOD FOR ASSESSING THE STRENGTH OF HAND AND FOOT MUSCLES

F. H. LEWEY, M.D., W. G. KUHN, Jr., M.D., and J. T. JUDITSKI

SATISFACTORY examination and periodic re-examination of large groups of patients with injuries to the peripheral nerves calls for a standardized method of measuring muscle strength. The method should be simple and rapid. The results should be reproducible and permit, in the hands of different examiners, the accurate evaluation of change in function. This is clearly a practical problem, in contrast to the physiologic attempts to determine in the strict sense, the power of a single muscle in foot-pounds or kilogram-meters. Hence, no reference will be made to this literature.

Our interest was concentrated on the muscles of hand, fingers, foot and toes. It was our desire to measure, instead of estimate, the resistance a patient could muster by contracting a group of muscles supplied by one nerve trunk. We decided to explore the reliability and the reproducible character of measurements obtained with the common spring-scale, a device readily adapted to the movements of the extremities.

From the Neurologic-Neurosurgical Sections, Cushing General Hospital, Framingham, Mass. and the Department of Neuroanatomy, Graduate School of Medicine, University of Pennsylvania.

Lovett, studying patients with infantile paralysis, seems to have been the first to make systematic use of the spring-scale for measuring muscle function. Martin, on Lovett's suggestion, developed the method in the Physiological Institute of Harvard. Tables of standard muscle strength were established for all groups of muscles of normal children for ages from 4 to 16 years. "Successive tests at short intervals showed the readings as to individual muscle groups to be in a large percentage of cases remarkably constant." Pollock used this method in nerve injuries during the first world war. Unfortunately, no one seems to have followed his good example.

The figures gained in our examinations would be of limited practical value unless expressed in percentage of a certain norm. This brought up the old question of the yardstick of normalcy. At first, we took for comparison, the corresponding muscle group of the patient's normal side. This doubled the time of examination and gave altogether unsatisfactory results since some patients had developed unusual muscle strength on the normal side as a compensatory factor.

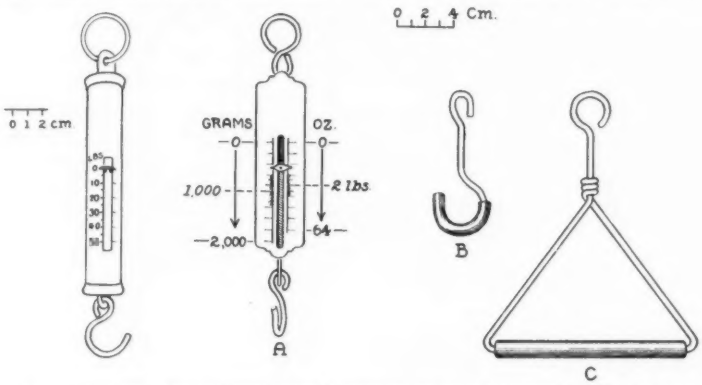


Fig. 1. Spring scales and appliances for measuring muscle strength. For their application see Figures 2 to 5.

TABLE I.— AVERAGE STRENGTH OF MOTIONS OF A HOSPITAL POPULATION EXPRESSED IN POUNDS (450 GRAMS)

		Mean M	Standard deviation of Mean SD_M	Standard error of mean SE_M	Range for normals $M \pm 2SD$
Upper Extremity					
Median nerve — Index	Flexion, end phalanx (flexor digiti profundus)	12.2	1.2	.2	10—14½
Thumb	Flexion, end phalanx (flexor pollicis longus)	12.4	1.0	.15	10½—14½
	Flexion prox. phalanx (flexor pollicis brevis)	21.3	2.5	.25	16½—26½
	Volar abduction (abductor pollicis brevis)	11.9	1.2	.3	9½—14½
	Opposition (opponens)	17.4	1.2	.3	15 —20
Wrist	Flexion	30+			
Ulnar nerve	Flexion, end phalanx (flexor digitorum profundus)	12.2	1.2	.2	10 —14½
Little finger	Abduction (abductor digiti quinti)	8.9	.6	.12	8 —10
	Adduction (adductor digiti quinti)	2.3	.6	.1	1 — 3½
Index	Abduction, first (interossei)	9.0	.8	.13	7½—10½
	Adduction	4.1	.4	.1	3½— 5
Thumb	Adduction	10.4	1.0	.2	8½—12½
Radial nerve — Wrist	Extension	30+			
Fingers	Extension, proximal phalanx (extensor digitorum communis)	11.8	1.4	.22	9 —14½
Thumb	Extension, distal phalanx (extensor longus)	8.8	1.7	.17	4½—12
	Extension proximal phalanx (extensor brevis)	13.4	2.1	.2	9 —17½
	Radial abduction (abductor pollicis longus)	11.0	1.2	.3	9½—14½
Lower Extremity					
Tibialis posterior nerve — Toes	Flexion	19.3	.2	.2	19 —20
Foot	Flexion (plantar flexion)	40.4	1.9	.2	36½—44
	Inversion (tibialis posticus)	20.8	2.0	.2	17 —25
Peroneal nerve — Toes	Extension	15.8	1.9	.2	12 —19½
Foot	Extension (dorsiflexion) (tibialis anticus)	30.5	1.9	.2	27 —34
	Eversion (peroneus longus and brevis)	20.6	1.7	.2	17½—24

Right-handedness and left-handedness had to be considered, as well as the general muscular development in manual workers, in contrast to clerical workers.

It seemed impractical to compute a mean for each professional group, and to select from the several means the correct standard for each examinee. We decided to determine the means (M) of the strength of various muscle groups, their standard deviations (SD) and standard errors (SE) in a hospital population which as a group, did not show the fitness of combat soldiers. The random sample consisted of persons showing no nerve or muscle weakness and included manual and clerical workers, as well as right-handed and left-handed persons (Table I).

To minimize the unavoidable variations, a standard method for measuring muscle function in patients with nerve injuries was developed. The method proved clinically adequate in use with more than 1,000 patients during a period of 2 years, and the norms were found to be satisfactory, provided that a standard technique of examination and a few precautions were used. We believe that our results, as tabulated, permit a sufficiently accurate and rapid method for determination of the extent of motor nerve damage and of the progress of its recovery.

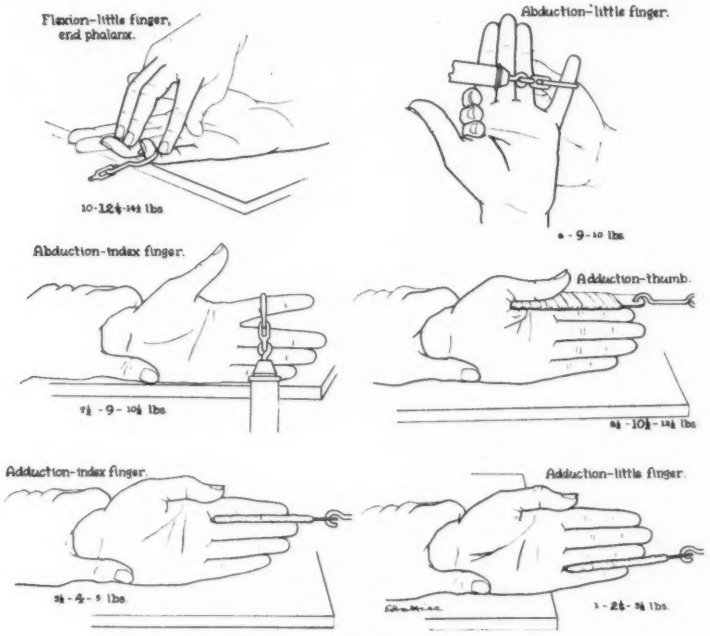


Fig. 2. Ulnar nerve.

Figs. 2–5. Standard position and fixation of hand and foot and direction of traction for measuring the strength of various characteristic movements. They are devised to prevent trick movements and minimize interference of auxiliary muscles. Presence or absence of contraction of the corresponding muscles has to be verified by inspection and palpation. The large figure indicates the mean strength of a hospital population, the small figures the range (± 2 SD), expressed in pounds (450 grams).

A METHOD FOR MEASURING MUSCLE POWER IN THE HAND AND IN THE FOOT

The apparatus used by us for these measurements are: (1) a spring scale indicating up to 50 pounds and calibrated against a certified scale; a small scale with a 64 ounce capacity is handy for measuring the first appearance of strength in hand and finger muscles; (2) a wire about 3/16 inch thick and about 4 inches long, one end of which is bent to hook into a ring of the scale, the other end bent into an open loop of about 1¾ inch diameter, covered with a rubber tube; (3) the same type of wire formed into an isosceles triangle of 4 inches length, the base of which is padded with rubber, the opposite tip bent to hook into the scale; (4) a thin metal plate about 4 inches long and 1 inch wide with a hole in one end for the scale. The plate is wrapped in tape to give a good grip. These fittings are shown in Figures 1 and 2.

Directions. The patient is informed of the principles of the method and admonished energetically and repeatedly during the entire examination to apply all possible force in resisting the pull of the scale. Hand, fingers, or leg have to be fixed by the examiner in such a manner that the patient is prevented from pulling with arm and leg instead of using the muscle groups under scrutiny. Figures 2 to 4 show the procedure in testing the forearm, hand, or finger muscles. In the foot, plantar and dorsal flexion of foot and toes, eversion and inversion of the foot are tested (Fig. 5). This same method could be applied for measuring other muscle groups in the arm and leg.

It is important to hold hand, fingers, and foot, respectively, exactly as indicated and to

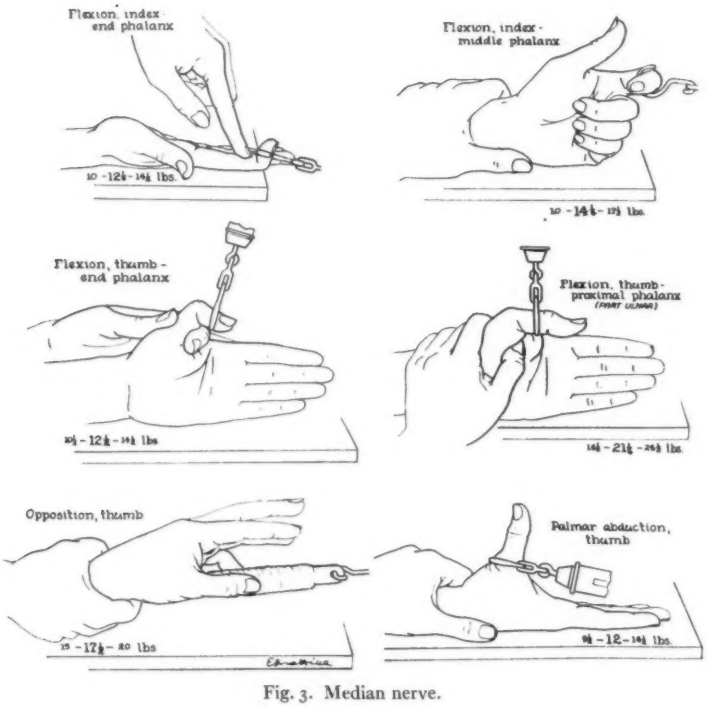

Flexion, index - end phalanx
10 - 12½ - 14½ lbs.
Flexion, index - middle phalanx
10 - 14½ - 17½ lbs.
Flexion, thumb - end phalanx
Flexion, thumb - proximal phalanx
(FIRST CLAWS)
Opposition, thumb
15 - 17½ - 20 lbs
Palmar abduction, thumb
9½ - 12 - 14½ lbs.

Fig. 3. Median nerve.

exercise traction in the given direction. Patients develop unconsciously innumerable trick movements and learn to use auxiliary muscles. The positions of extremities, hook and scale have been so chosen as to exclude—as far as possible—such undesirable errors, e.g. the contraction of the finger extensors in testing abduction of index or little fingers. Nevertheless, inspection and palpation of the muscles or muscle groups under scrutiny should not be omitted.

The results were recorded, either directly in pounds or in percentage of the normal, depending on the purpose for which they were used (Figs. 6 to 8). The large figure (M) was used to compute the percentage of deviation from the norm. The range (small figures, $\pm$ 2SD) gives a general idea of what strength can be expected in a certain movement. The pounds given on Figures 2 to 5 are slightly at variance with those of Table I. They are rounded to a quarter of a pound in contrast to the calculated values of Table I.

The unit of measurement was noted on each chart with the date and name of the patient and the examiner. We found special remarks sometimes useful, e.g. that the patient did or did not apply maximal force, that he seemed to be in good or poor condition, that it was a very hot day, etc.

Figure 6 gives an example of loss and gradual improvement of function following severance and suture of the median nerve at the wrist. There was no function in any of the hand muscles when first examined 3 months after suture of the nerve. In addition, there was a mild weakness from disuse in the ulnar musculature. At the time of the last examination, 14 months after operation, all intrinsic muscles innervated by the median nerve were active with the exception of the abductor pollicis brevis which frequently fails to return. The end phalanx of the index finger could not be moved because of partial ankylosis. The ulnar innervated muscles had returned to almost normal strength.

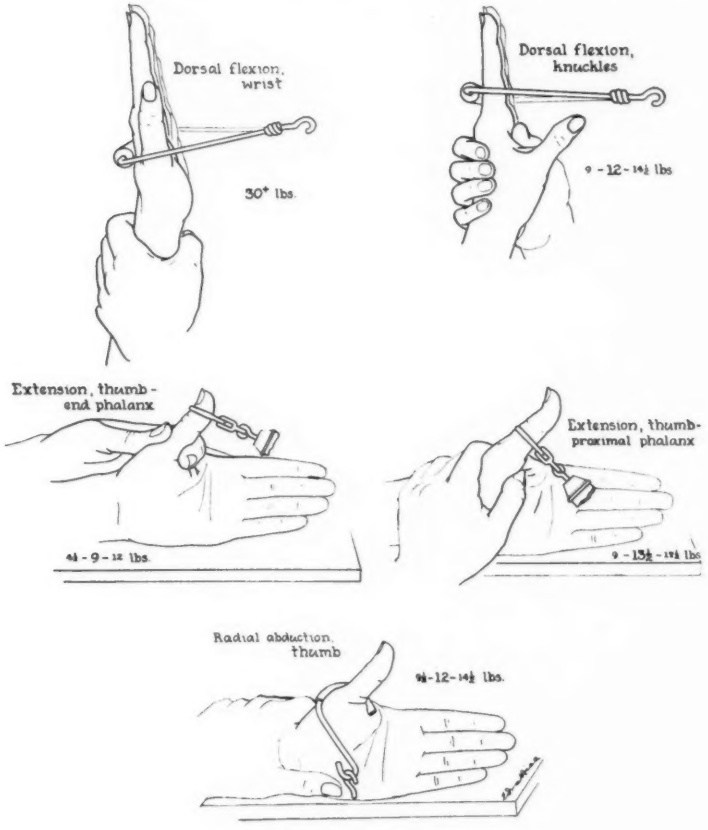

Dorsal flexion, wrist
30+ lbs.
Dorsal flexion, knuckles
9 - 12 - 14½ lbs
Extension, thumb - end phalanx
4½ - 9 - 12 lbs.
Extension, thumb - proximal phalanx
9 - 13½ - 17½ lbs
Radial abduction, thumb
9½ - 12 - 14½ lbs.

Fig. 4. Radial nerve.

Figures 7 and 8 record the course of an ulnar nerve paralysis and lysis in the middle of the forearm. Figure 7 shows the increasing strength in pounds, Figure 8 in percentage of the norm. The last illustration of this figure indicates practically full return of function in all muscles with the exception of the abductor indicis. This muscle was seldom used in the patient's work. The abductors of the first and second fingers seem to be innervated by a twig from the median nerve.

This form of recording gives at any time an immediate survey of the progress of recovery following a nerve lesion and a survey of the functional deficit in percentage of the norm.

DETERMINATION OF RELIABILITY OF THE METHOD

Controls. It remained to demonstrate what degree of reliability could be expected from measuring the strength of voluntary muscle contractions by means of the spring scale with the described precautions. A comparative study was made for this purpose on the abductor digiti quinti muscle in 76 patients with ulnar nerve lesions. The strength of this muscle and its gradual increase over a longer period of time was determined in sequential examinations and expressed in percentage of the normal. Simultaneously, the electromotive force (EMF) generated by this muscle on maximal electrical stimulation of the ul-

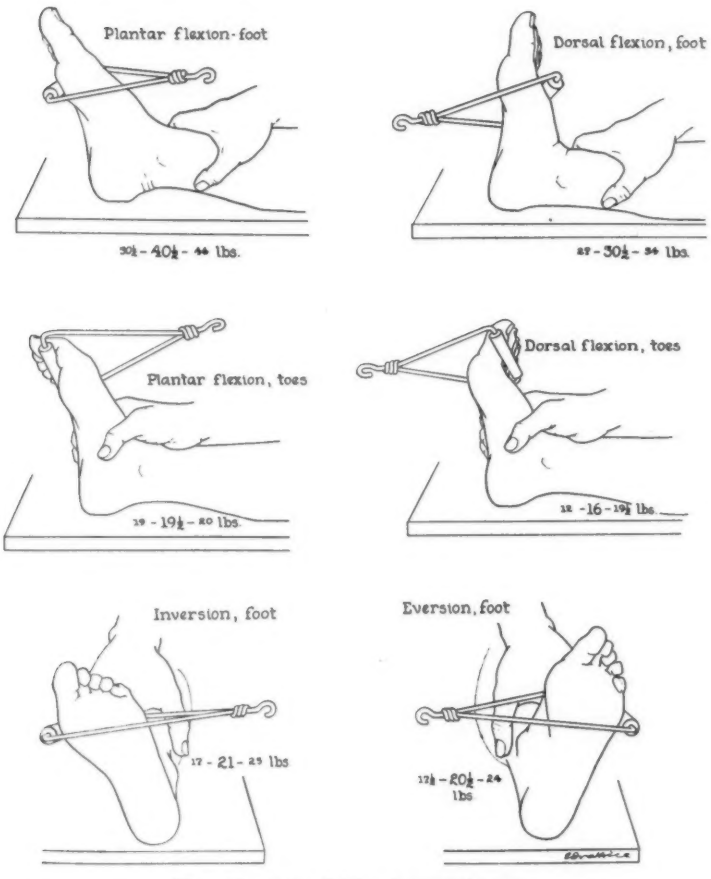

Plantar flexion-foot
30½ - 40½ - 44 lbs.
Dorsal flexion, foot
27 - 30½ - 34 lbs.
Plantar flexion, toes
19 - 19½ - 20 lbs.
Dorsal flexion, toes
12 - 16 - 19½ lbs.
Inversion, foot
17 - 21 - 25 lbs
Eversion, foot
17½ - 20½ - 24 lbs

Fig. 5. Posterior tibial and peroneal nerves.

nar nerve (amplitude of electromyogram) was measured in millivolts and expressed in percentage of the value obtained on the normal side of the patient. This procedure may be called an objective method. The values obtained by the two methods of examination were plotted against each other. The scatter diagram (Fig. 9) shows a high degree of relationship ($r = +0.79$) between (1) the EMF on maximal nerve stimulation and (2) the strength of voluntary contraction, both expressed as percentage of normal, in the same muscle at the same time. A standard error of 0.04 indicates that "r" departed highly significantly from zero.

We were interested in this context in the reliability of the percentage values of voluntary strength. Strength was, therefore, chosen as the dependent variable (Y). The standard error of estimate in Y ($^{\sigma}Y_{e}$) was found to be 12.7 per cent. RR is the least squares regression line.[1] The bands of normality on each side, $2^{\sigma}Y_{e}$ (25.4%), are shown as dotted lines. This permits one to estimate or predict the value of strength (Y) if the EMF (X) is known. Insert the determined value of EMF in per cent of the normal on the abscissa, follow this line up to the point where it bisects

[1]The meaning of the Y intercept (OR) will be discussed in another context.

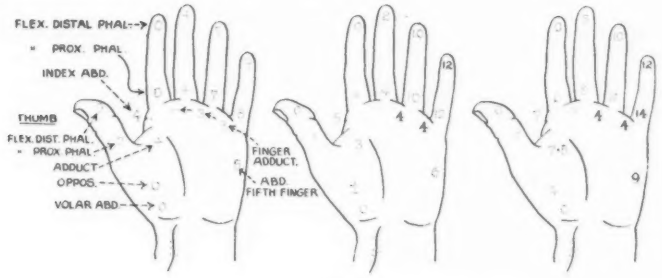


Fig. 6.

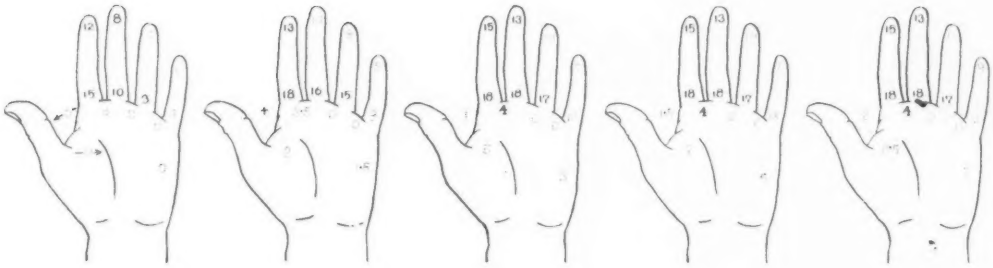


Fig. 7.

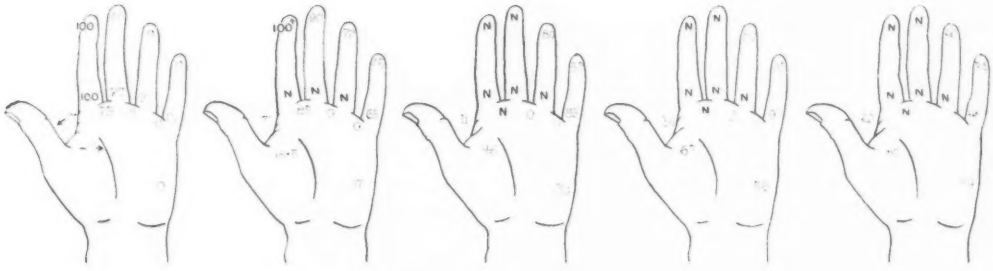


Fig. 8.

Fig. 6. Three stages of improving muscle strength in a patient with median nerve interruption and suture above the wrist. From left to right: 3.6 and 14 months after suture. The first picture explains to which motions the standard location of numbers refers. Dotted numbers, originally written in red, indicate deficient strength. Strength in pounds (450 gm.).

Figs. 7 and 8. Four stages of improving muscle strength in a patient with paralysis and neurolysis of ulnar nerve at middle of forearm. The four pictures represent the time before operation, 3, 6, 9, and 12 months following neurolysis. Figure 7 gives the strength in pounds (450 gm.), measured with help of a scale, Figure 8 in percentage of normal. For details see legend of Figure 6 and text.

the regression line and read the predicted value of strength in per cent of the normal on the ordinate.

The 0.99 fiducial limits of the coefficient of correlation are between 0.61 and 0.89. This means that, taking an indefinitely large number of persons homogeneous with the 76 actually examined, it is highly likely that the coefficient of correlation will fall within the limits of 0.61 and 0.89.

The scatter diagram shows 72 out of 76 or, approximately 95%, of all points falling with-

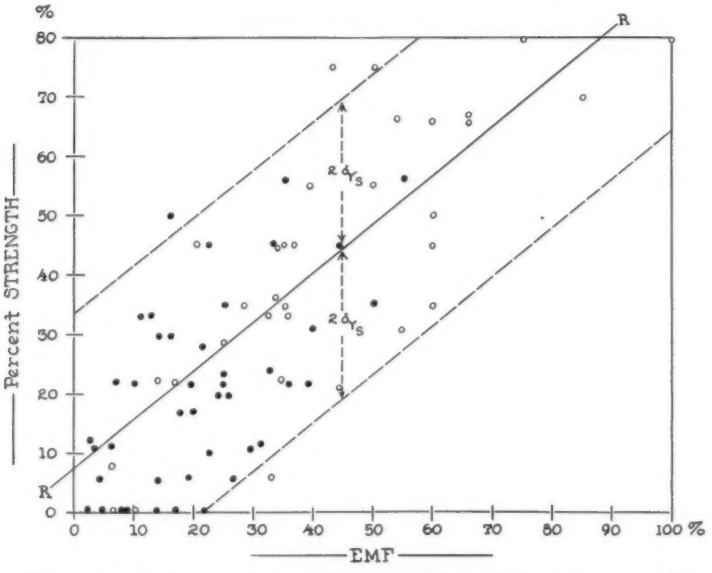


Fig. 9. Scatter diagram of strength in the abductor digiti quinti, measured by means of a spring scale and expressed in percentage of the normal, plotted against the electromotive force generated by the same muscle on maximal stimulation of ulnar nerve at elbow, measured in mV (amplitude of electromyogram) and expressed in per cent of the corresponding value in the patient's normal arm. Full dots, nerve sutures. Open rings, neurolysis. RR, fitted regression line with the bands of normality on each side. σY_s, standard error of estimate in Y.

in the limits of $RR \pm 2\sigma Y_s$. This percentage corresponds very closely with the results expected when a straight regression line is appropriate to the data and when the points are normally distributed around the line. We may therefore use this line and the limits of $RR + 2\sigma Y_s$ as the normal region. If a point falls outside these limits, it is likely that there is something extraordinary about the patient. If the point lies above the upper limit, we have no interest in the extraordinary cause in this paper. If it lies below the lower limit, it is legitimate to take the result as an indication of inadequate voluntary contraction. The method here developed seems pertinent to the problem; but more reliable values for $RR + 2\sigma Y_s$ could be obtained from enlarging the sample.

The results of the spring scale method may, therefore, be called reasonably reliable, reproducible and comparable. Furthermore, Figure 9 gives a reasonable basis of action until larger studies are made. The measurements provide a good record of individual return of muscle strength from zero to one hundred per cent, or wherever the curve levels off.

Limitations. The values obtained with this method are approximations. Differences of less than one-half pound should be considered —as far as our experience goes—within the range of the experimental error in the small hand muscles, whereas differences of 1 or 2 pounds may be neglected in the stronger muscle groups. Hence, not much change could be expected from examinations at short intervals in the case of a regenerating nerve. Our routine examinations were spaced 2 to 3 months apart, beginning as soon as the first signs of returning function were observed.

SUMMARY

A standardized method of measuring the function of various muscle groups in hand, fingers, foot, and toes by means of a spring

scale, its validity, and limitations are described. The mean and its standard deviation have been computed for these muscle groups, permitting the expression of the original values in percentages of the normal for an average hospital population. The method was checked against an objective examination (electromyogram) and proved valuable for following graphically the returning muscle strength after nerve injuries with and without nerve suture. Such curves come in handy in cases of delayed improvement or unexplained weakness and in assessing the per cent of actual muscle power at a given time.

REFERENCES

1. LOVETT, R. W. The Treatment of Infantile Paralysis, pp. 163-171. Philadelphia: Blakiston Sons, 1917.
2. MARTIN, E. G., and LOVETT, R. W. J. Am. M. Ass., 1915, 65: 1512.
3. POLLOCK, L. J., and DAVIS, L. Peripheral Nerve Injuries. New York: Paul B. Hoeber, 1933.

ACUTE PANCREATITIS

II. An Experimental Study with Special Reference to X-ray Therapy

TAGUE C. CHISHOLM, M.D., Minneapolis, Minnesota, and ROY E. SEIBEL, M.D., Buffalo, New York

IT is now commonly recognized that the method of choice for treating acute nonsuppurative parotitis is with roentgen rays. About 1938 Morton and his coworkers in Rochester, New York, were struck by the interesting analogy between the parotid gland and the pancreas: both of these glands were of the serous type and blood amylase levels were elevated with disturbances of either. In 1940 Morton and Widger, encouraged by their early experiences with the roentgen treatment of acute pancreatitis, published their first clinical report. In 1945 we reviewed the clinical and pathological records of the 8 cases of acute pancreatitis treated by roentgen therapy in the Peter Bent Brigham Hospital in Boston together with the 13 cases then reported in the literature(1). The series was too small and the available data too scanty to draw any conclusions. In an endeavor to place the x-ray treatment of acute pancreatitis on a factual, rather than an empirical, foundation the following experimental studies were undertaken.

METHOD

In order to create acute pancreatitis in our investigation we adopted the method described by Rich and Duff in 1936 in their classical study on the pathology of experimental pancreatitis in dogs. Under nembutal anesthesia[1] the second portion of the duodenum was opened. The duct of Santorini was cannulated with a blunt No. 25 needle, and bile, freshly aspirated from the gall bladder, was injected into the pancreas. When less than 2 cubic centimeters of bile was slowly injected into 16 kilogram dogs at a pressure lower than 18 centimeters of water, the ductal tree of the pancreas was filled but not ruptured. In a matter of a few minutes acute edema of the pancreas immediately developed while the organ was under direct vision (Fig. 1). The lobules became widely separated by a transparent transudate which microscopically showed a few extravasated leucocytes but primarily an interacinar edema. When 2 to 10 cubic centimeters of bile was as rapidly injected into dogs at a pressure over 18 centimeters of water the ductal tree of the pancreas was ruptured, the immediately visible interlobular edema became bile tinged (Fig. 2) and in a matter of a few minutes small petechiae appeared in the acinar substance. Microscopically the pancreas at this time displayed large numbers of extravasated erythrocytes, leucocytes, fibrin, and granular débris. Several hours after the injection of bile this type of pancreas (Fig. 3) showed numerous yellow plaques of fat necrosis, both in the substance of the pancreas and on the omentum, mesentery, and peritoneal surfaces.

RESULTS

Figure 4 shows the curves of serum amylase levels from 10 acute experiments over a 12 hour period. After the induction of acute pancreatitis, blood samples were periodically taken until the dogs were sacrificed. The solid lines represent steadily rising serum amylase levels in dogs which displayed severe necrosis at autopsy. The broken lines represent less acute rises in serum amylase levels in dogs which showed only edema at autopsy. The former received 2 to 10 cubic centimeters of bile under great pressure, thus rupturing the ductal tree. The latter received less than 2 cubic centimeters of bile under mild pressure and showed no extravasation of bile outside the pancreatic ducts. In the former, blood amylase levels continued to rise until the end of the 12 hour period of observation, while in the latter, during the same interval, serum

From the departments of surgery and radiology, Peter Bent Brigham Hospital, and from the Laboratory for Surgical Research, Harvard Medical School. Dr. Chisholm, Arthur Tracy Cabot Fellow in the Laboratory for Surgical Research; Dr. Seibel, Resident in Radiology, Peter Bent Brigham Hospital.

[1]Dosage: 32 milligrams per kilogram administered intravenously.

amylase was either approaching or had returned to normal levels.

Figure 5 shows the curves of serum amylase levels from 10 acute experiments followed over a 7 day period. These operations were done with aseptic precautions and blood sampling was conducted periodically until the dogs were sacrificed. Again the solid lines represent animals receiving injections of large amounts of bile under increased pressure; these dogs uniformly sustained quite high serum amylase levels which only slowly fell toward normal. At autopsy they showed varying stages of subsiding pancreatic necrosis. The broken lines represent dogs receiving injections of less than 2 cubic centimeters of bile under low pressure in which amylase levels rose to less high levels, returned to normal sooner than in the companion series and at necropsy showed only the end results of an acute edema of the pancreas.

The next objective of the study was to ascertain what was the response of the normal pancreas to x-ray therapy as reflected by alterations in the blood amylase levels. Figure 6 indicates the response in 6 dogs to a single treatment of 90 r each (represented by the solid lines) and in 5 dogs to 200 r each (represented by the broken lines). These doses were delivered over a 15 square centimeter area of the epigastrium with a skin target distance of 50 centimeters, a peak kilovoltage of 200, a

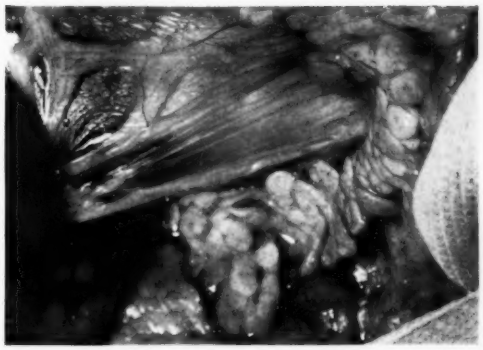


Fig. 1. Acute edema of the pancreas a few minutes after gentle retrograde injection of bile into the duct of Santorini.

Fig. 2. Acute edema of the pancreas with petechial hemorrhages a few minutes after vigorous and rapid retrograde injection of bile into the duct of Santorini.

Fig. 3. Acute necrosis of the pancreas a few hours after vigorous and rapid retrograde injection of bile into the duct of Santorini.

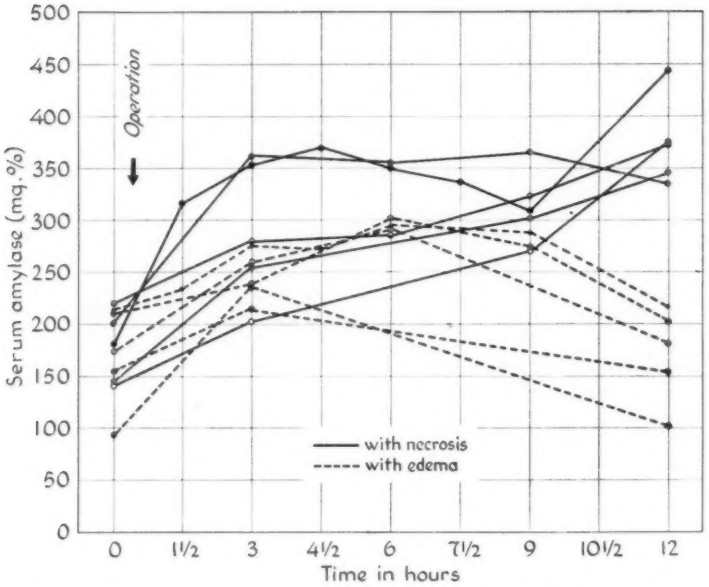


Fig. 4. Serum amylase curves over a 12 hour period following the experimental induction of acute pancreatitis.

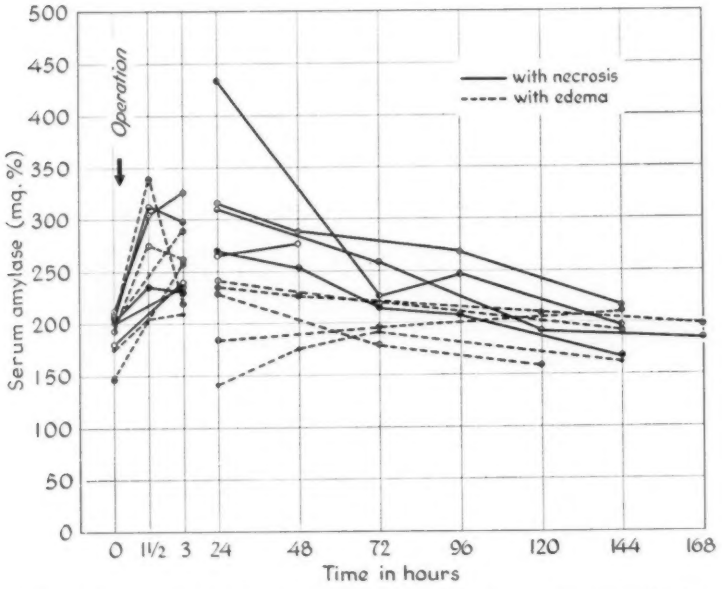


Fig. 5. Serum amylase curves over a 7 day period following the experimental induction of acute pancreatitis.

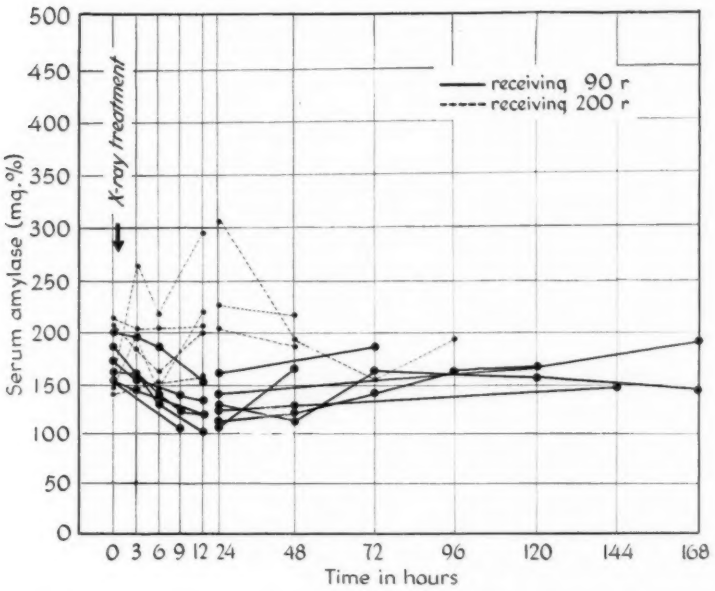


Fig. 6. Serum amylase curves over several days following the exposure of the normal pancreas to a single treatment of x-rays.

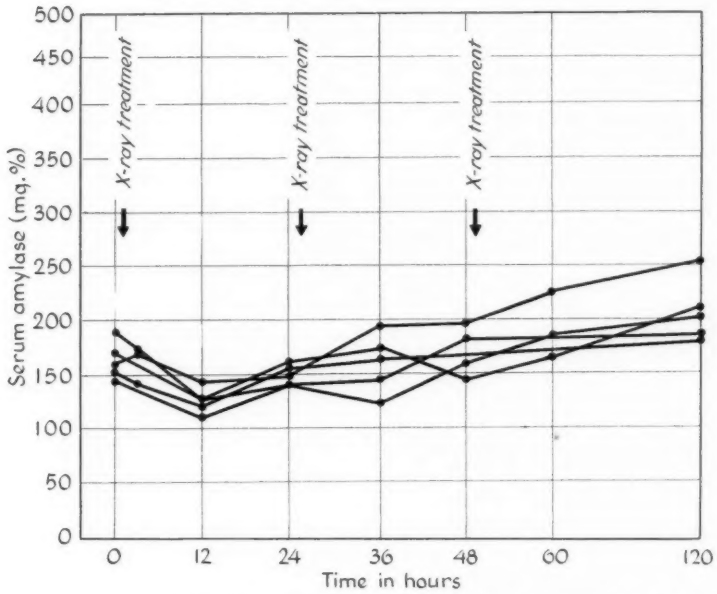


Fig. 7. Serum amylase curves over several days following serial exposures of the normal pancreas to divided doses of x-rays.

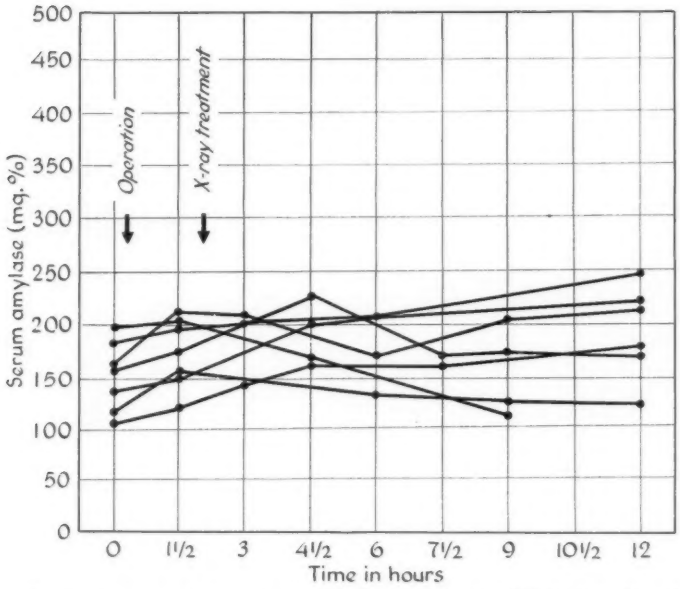


Fig. 8. Serum amylase curves over several days following first the induction of acute pancreatitis, and second, the exposure of the pancreas to a single x-ray treatment.

filter of 1 millimeter of aluminum and ½ millimeter of copper, and 18 milliamperes. Of the series receiving only 90 r, all had direct drops in serum amylase levels over a 12 hour period with return to or toward normal in 2 to 5 days. At the time of autopsy every pancreas of this series showed subsiding hypermia but no edema or necrosis. Those dogs receiving 200 r in a single treatment displayed responses with great variations in the serum amylase titers. A few of the larger animals had drops corresponding to the series receiving 90 r. The smaller dogs, however, showed irregular rises in serum amylases and at autopsy had acute edema, petechiae, and tiny foci of fat necrosis.

Since both Morton (2) and the radiology service in the Peter Bent Brigham Hospital had frequently employed a series of three consecutive treatments in their human patients with acute pancreatitis, we investigated the serum amylase response of normal dogs to three consecutive exposures, 24 hours apart, of 90 r each. Figure 7 illustrates our findings in 5 dogs. There was a uniform depression of serum amylase levels after the first treatment but with the second and third exposures a diffuse hyperemia with edema ensued. A few showed tiny foci of necrosis. All dogs in this series showed a steady rise in serum amylase levels after the second exposure to roentgen rays.

Finally, we combined the aforedescribed methods of, first, creating acute pancreatitis, and, second, immediately giving these subjects a single treatment of 90 r to the epigastrium. Seven dogs from this series are represented on Figure 8. All were given sufficiently large injections of bile to create pancreatic necrosis. Although more experiments must be carried out in this manner before irrefutable conclusions can be drawn, nevertheless, it is of interest to note that in not a single instance did the serum amylase titers rise anywhere nearly as high as in the original series without x-ray treatment. Yet at autopsy all of these dogs showed moderately severe pancreatic necrosis.

COMMENT

On the basis of the above described limited number of observations on experimentally induced acute pancreatitis with and without

x-ray treatment it appears warranted to conclude that too large a dose of roentgen rays may well defeat the purpose for which it is administered, i.e., to inhibit enzyme production in the already damaged pancreas. Furthermore it is suggested by the aforedescribed studies that repeated serial exposures of x-rays to the pancreas may well have a cumulative effect as deleterious as an initial heavy exposure. And finally that an appropriately small single dose of roentgen rays administered to dogs having experimentally induced pancreatic necrosis appears to inhibit amylase enzyme production with minimization of pancreatic tissue destruction. The application of these observations to the roentgen treatment of acute pancreatitis in humans is clearly suggested.

SUMMARY

1. Observations are reported on the pattern of serum amylase curves in dogs with experimentally induced acute pancreatic edema and acute pancreatic necrosis.

2. Similar observations are reported following periods of x-ray treatment to the normal pancreas.

3. Other observations are reported on the behavior of the serum amylase curves in dogs receiving acute experimental pancreatic necrosis followed immediately by a single x-ray treatment of 90 r.

4. And finally, the application of these observations to the roentgen treatment of acute pancreatitis in humans is discussed.

REFERENCES

1. CHISHOLM, TAGUE C., and SEIBEL, ROY E. Acute Pancreatitis. I. A Clinical Study with Special Reference to X-ray Therapy. (In press.)
2. MORTON, JOHN J., and WIDGER, STANLEY. Ann. Surg., 1940, 111: 851.
3. RICH, A. R., and DUFF, G. L. Bull. Johns Hopkins Hosp., 1936, 58: 212.

EDITORIAL

SURGERY
Gynecology and Obstetrics

FRANKLIN H. MARTIN
Founder and Managing Editor
1905-1935

LOYAL DAVIS, Editor

Associate Editors
SUMNER L. KOCH MICHAEL L. MASON
M. E. SPENCER, Assistant Editor
Editorial Staff Associates
DONALD C. BALFOUR JAMES T. PRIESTLEY

DECEMBER, 1947

FUTURE SURGEONS

FOR a hundred and fifty years in this country surgical training was for the most part informal and vague. Over the past five decades various patterns that one might follow to become a surgeon have evolved. In the last twenty years these have become more distinct, with the result that surgical training has been defined and standards established. He who embarks on a career of surgery is confronted with a protracted period of training after graduation from medical school. Heretofore, the surgeon after a long period of residency or apprenticeship with little or no income could expect to receive in a relatively short earning period, and by the time he had reached the age when he could no longer work, compensation that would equal the total income of his medical confreres. Thus, his family, although often an addition of his later life, had security and provision for education. Today, taxes and the trend of fees make the annual net income of the surgeon during his most active periods of practice so limited that he cannot set aside appreciable savings that will compensate for the long lean years of preparation or provide for his old age.

As medical school graduates continue to embark on surgical careers with an eye to their immediate and future livelihood, they will require and seek a reasonable subsidy during this training period. If incomes are to be limited, a subsidy should be available during the many years of preparation which are required. The cost may be borne by the hospital, the community, or the state. Surgery and its specialties, more than other divisions of medicine, demands intensive and prolonged training. The present generation has seen those who are now its leaders of surgery struggle through such training. The merit of the system for a few in the past is undeniable, but for the majority, both for the present and the future, its applicability is questionable.

In this present period after the second World War it appears that many changes may be anticipated. The continuity of trends prior to the war were interrupted and now after the many surgeons who were in the service have returned, new problems become evident. These changes involve all of medicine. There is a strong trend toward hospital practice. Almost every community is planning an increase in the number of its hospital beds and those up to now without hospital facilities are contemplating building them. In the future, a greater number of surgeons will be required. The actual standards of surgery will depend upon the training these surgeons of the future receive.

The emphasis in the building of hospitals has been on the physical plant and equipment.

This is important, but more important is the hospital staff, which should be continually improved. The quality of the work done by a staff is dependent on the training of its members. There are many large hospitals in the country that have competent and well trained men who take excellent care of patients but who contribute little or nothing to the instruction of those in training. This is particularly true in municipal, county, and private hospitals located in towns and cities without medical schools. The community should be concerned with the cost of the staff as well as the building and its equipment. A subsidy is needed to pay certain members of the senior staff to carry out a training program, and to provide the surgeon in training a sufficient income so that he can maintain a social position equal to that of his peers in other professions.

In effect, it is proposed that all hospitals become teaching institutions, that they serve as the medical centers of the community. Today it is unfortunately true that some small hospitals, so far as surgery is concerned, may be a liability to a community rather than an asset. Surgeons should be interested in a policy that provides for hospitals of sufficient size, properly equipped and staffed to do adequate and sound surgery. The resident system of training in surgery as now employed in many of the university medical centers, modified to meet local circumstances, might well be utilized throughout the country to the advantage of the future surgeons and their patients. Such a plan should materially increase the number of properly trained surgeons who will be needed in the future and, of equal importance, it will stimulate the surgeons associated with these hospitals to keep abreast of advances and create channels through which new information can be easily circulated. Benefits that may accrue will be of greatest value to the citizens of the community in which these hospitals function.

The various insurance schemes for hospitalization have gained great popularity over the last few years and the trend continues. These programs, in a period of economic prosperity, have been accompanied by a decrease in the number of patients occupying teaching beds. Many hospitals dependent on endowment for support have had a reduction in income and an increase in operational expense. Many hospitals consequently have embraced the insurance plans. As a result, ward services have been curtailed and clinical material for training purposes has been reduced. This is unfortunate because patients are benefited when properly used for teaching purposes. The majority of well-staffed hospitals could evolve a plan whereby patients who are insured would be taken care of by the senior and resident staffs and at the same time be used for teaching purposes.

Surgeons should understand the problems that confront the medical school graduate as he views surgery as a possible career. The value of a long, thorough training in properly staffed and equipped hospitals with adequate clinical material is evident to surgeons but requires emphasis to the profession and laity. The cost of training professional personnel in a hospital should be looked upon as one of the best long time investments that the community which supports that hospital can make.

FRANK GLENN.

THE SURGEON'S LIBRARY

THE BOOK SHELF

VIENNA 1947

ALEXANDER BRUNSCHWIG, M.D., F.A.C.S., New York, New York

DURING the past summer a mission was sent to Austria by the Unitarian Service Committee under auspices of the World Health Organization (Interim Committee). There were eight members from the United States representing: physiology (Vissher, University of Minnesota), pharmacology (Cattel, Cornell) cancer research (Bittner, University of Minnesota), internal medicine (Chester Jones, Massachusetts General Hospital and Harvard), psychiatry (Wortis, New York University), general surgery (Brunschwig, Memorial Hospital and Cornell), neurosurgery (Joseph Evans, University of Cincinnati), anesthesiology (Stewart Cullen, Iowa State University College of Medicine). There were two Swiss members, Prof. Alfredo Vannoti (Lausanne) internal Medicine, and Prof. Herman Mooser (Zurich) hygiene and public health. The purpose of the mission was to acquaint the Austrian medical profession with advances in various fields that had been made in America and Switzerland since 1939 when scientific communication between Austria and the outside world was almost completely cut off, and to receive information regarding progress made in the Austrian clinics during this period. This plan was carried out by means of lectures, informal conferences, ward rounds, and operative work on the part of the mission members.

Because of the large number of American surgeons who attended for varying periods the clinics in Austria, especially Vienna, the writer summarizes in the following paragraphs the situation in Austria, as observed during the aforementioned voyage.

The Allgemeines Krankenhaus is essentially undamaged and the general activity is quite similar to what was observed by the writer in 1931. The first surgical clinic is headed by Professor Schoenbauer who is active in general surgery and does the neurosurgery for this and other hospitals as well. The second surgical clinic is headed by Professor Wolfgang Denk, and is traditionally "The Clinic of Billroth." The author had the privilege of examining the preserved specimen of Billroth's first pylorectomy for carcinoma. Professor Denk is especially interested in thoracic surgery and has recently begun to do total pneumonectomies and transthoracic gastroesophagectomies. He is also Dean of the Medical Faculty. Professor Finsterer is working as hard as ever, and continues to direct his *abteilung*. His seventieth birthday was recently celebrated by a public ceremony at the hospital. Professor Kahr is head of the first gynecological clinic (Wertheim's clinic) and Professor Antoine is head of the second gynecological clinic (Schauta's clinic). Dr. Schoenbaur is also head of the Institute of Medical History, and during the war period his book concerning the history of the Medical Faculty of Vienna was published. This is a beautifully written and illustrated book which will prove a standard reference in years to come.

The shortage of catgut is so acute that silk and linen suture material are used almost exclusively. The supply of rubber gloves is also short and this necessitates the use of cotton gloves; in some clinics no gloves are used. The author had the experience, quite arresting for an American, of operating without gloves, and once over the initial surprise, it afforded the impression that dexterity was facilitated. There is no shortage of surgical instruments in the operating rooms.

Blood banks are nonexistent. Transfusions, when given (which appears to be not very often), are administered by the direct method. One or two donors are held in a room adjacent to the operating room and lie down on stretchers when utilized. Blood is drawn into a paraffinized Kimpton tube and brought quickly to the patient; the blood is run in by means of a large cannula previously inserted by cutting down upon a large vein.

Little stress is placed upon postoperative fluid balance, and in one large clinic there were no out-

From the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York.

fits for intravenous infusion by venipuncture. When such measures were to be carried out, a large cannula was inserted into a vein by the cut-down method. Sterile physiologic saline solution was generally available but dextrose solutions were not available due to the shortage of sugar. Vitamins C and K are available in limited quantities. No records of daily urine excretion are kept routinely. Continuous gastric aspirations by means of Levine tubes and suction does not appear to be practiced anywhere in Austria. Early ambulation is carried out irregularly.

Sulfa drugs are plentiful. Penicillin is obtainable in only limited quantities and often when it is requested there must be a bacteriological study to prove that the infective organisms are penicillin sensitive. Streptomycin is not available. Opium and its derivatives are not plentiful and indeed in some clinics were not available at all. Small quantities of thiouracil have been provided and a few patients have been treated with it.

The operative work observed was very high grade for the routine procedures. Few or none of the newer operations have been attempted. Total pneumonectomy has not been performed in Austria more than possibly six times, probably fewer transthoracic cardioesophagectomies have been done. No pancreatoduodenectomies have been performed. The heavy metal intramedullary pin (Kutchner pin) is frequently used in fractures of the femur and there appears to be satisfaction with the results. Prefrontal lobotomy has not been carried out. Irradiation therapy for carcinoma of the cervix has never been as extensively employed as elsewhere. Patients with Stages I and II (and often III) receive either the radical vaginal hysterectomy (Schauta) or the radical abdominal hysterectomy (Wertheim). The latter is carried out according to the original operation in which excision of parametrial tissue is emphasized but no attempt is made to remove extensively the lymph nodes along the great vessels of the pelvic wall. The wide use of the term "Wertheim operation" in the United States to indicate a very radical hysterectomy should be abandoned, as Wertheim did not conceive of the operation that is inferred by American surgeons and gynecologists (radical node resections). It was stated that the immediate surgical mortality is about 5 per cent for the Wertheim operation. No recent follow-up studies on results are available.

Peptic ulcer when first encountered is treated medically, but this regimen does not appear to be as rigid and vigorous as conceived by internists in the United States. When this has failed, resection is done. Duodenal ulcers are managed by Billroth II, Pólya, or Finsterer operations; gastric ulcers by Billroth I. The latter is performed with radical gastrectomy, and the surgeons appear satisfied with it, claiming few recurrences. In some instances, after gastrectomy, calomel tablets were placed in the opened small bowel to insure early evacuation of stool and reduce the incidence of distention and paralytic ileus.

Neoplasms of the colon are treated in several ways and there is a marked tendency for multiple stage excisions due to lack of penicillin, and poor nutritional state of these patients when they are admitted for treatment. Much of the operative work is done under local or spinal anesthesia. General anesthesia is given by junior assistants, who do not remain very long on this service. No physicians specialize in anesthesia but it is contemplated that specialization in the administering of anesthetics will develop.

Specialization in the various surgical fields is not extensively developed. While a rigid separation is made between gynecology and abdominal surgery, and the former is carried out by those who also are obstetricians, urology with its special instrumental armamentaria remains in the general surgical clinics and is the province of senior assistants who devote periods rotating on that service. Orthopedics likewise is not generally separated, although some surgeons are able to confine themselves to that field. Fresh fractures are taken care of in "traumatic stations" which are adjuncts to general surgical services. Neurosurgery has not developed as a special field, nor has thoracic surgery. In Innsbruck (Prof. B. Breitner) a surgeon limits his practice entirely to thoracic surgery (Dr. Kux) and another entirely to neurosurgery (Dr. Sargo). As mentioned, these situations are unique in Austria.

Experimental laboratories in connection with the surgical clinics have not been developed, and the surgeons have not become interested in some of the newer biochemical aspects of the surgical patient. For example, the surgeon there is not familiar with the concept of plasma proteins and their implication for the surgical patient; indeed, when the question was raised in connection with a patient undergoing an extensive operation, no facility was available for making this determination—it had never been done before in surgical patients. This instance serves as a concrete example of the misfortune resulting when a group of surgeons are more or less completely cut off from international literature and personal exchange of ideas with men from other countries.

The writer performed transthoracic cardioesophagectomies upon 2 patients with cardioesopha-

geal carcinoma—one of them was an extensive lesion which by usual criteria was classified as inoperable. The usual left transthoracic approach was made. The anesthesia was administered by Dr. Stewart Cullen. With no blood banks, and no special preoperative preparations, and with only physiologic saline solution for intravenous infusion, no data on plasma proteins, etc., and the patients in rather poor nutritional condition, both pursued essentially uneventful convalescences. One did not ingest fluid by mouth for 9 days and one not for 6 days. Such experiences, to the writer at least, raise the question if as result of a great enthusiasm for the best possible preoperative and postoperative supportive treatment, we in America often might not go beyond the necessary requirements, make extra work for ourselves and carry out measures which have certain minimal risks of morbidity and even mortality.

The Vienna faculty (as others in Austria) has been subjected to a very trying period since the end of the thirties. First, as a result of the *anschluss* there was a general purge of those who were not acceptable to the new regime because of racial background. Then followed the slower process of dislodging those whose ideological tenents were not "reliable." Then came the period of Germany's success on all fronts when the *Wehrmacht* appeared to be invincible; this strengthened the point of view of the new regime in Austria. Following this, came the failure of German arms at Stalingrad, the retreat and finally the allied victory. The latter lead to a new government in Austria with the institution of anti-Nazi proceedings against those held guilty of propounding the Nazi cause, and their removal from official positions pending the results of these inquiries and trials. It does not require a great deal of imagination to appreciate the difficulties for scientific work amid such disturbances which created conditions that profoundly affected the daily conduct of everyone.

REVIEWS OF NEW BOOKS

THE Danish Surgical Society conferred an award on Dr. Aalkjaer in 1944 for the first publication of *Fluids, Electrolytes and Protein in Surgery.*[1] Recently this handbook of 150 pages has been revised and reprinted and now an excellent English translation is available.

Dr. Aalkjaer has spent 10 years in developing a simple and practical routine for quantitative replacement of fluids, electrolytes, and protein in his general surgical and urologic patients. This manual is a direct and complete description of the reasons for this program and of the means by which it is carried out. As the basis for this progressive work he has used the conclusions of more than 100 authors writing on these subjects at the present time. The comprehensiveness of his approach and the reduction of the many problems to simple terms and usages is to be highly commended.

The book is arranged in three parts: (1) the normal physiology of the electrolyte-fluid-protein metabolism; (2) the pathologic physiology; (3) the clinical application. Under these headings the author describes first the fluid, electrolyte, and protein requirements of the body and the essential laboratory determinations, then the physiologic changes that occur, and finally the methods of quantitative correction of these changes. He clearly describes how quantitative replacement therapy can be used in a small hospital. Details are given as to adequate methods of laboratory analyses of protein, chloride, and carbon dioxide, preparation of fluids, collection of blood, and methods of administration. Excellent brief surveys on the differences of new and old bank blood, or the use of plasma in place of blood, and the use of new plasma substitutes such as dextran are given.

To facilitate replacement therapy in anemia, dehydration, acidosis, alkalosis, and shock, the author has reproduced many charts of other investigators, for example, Gamble, Van Slyke, Coller, and Maddock, and also from his own work. Case reports of interest in fluid or electrolyte or protein problems are frequently given with the addition of a simple chart showing daily laboratory and urine tests along with total output and total input. Interesting observations are made on uremia being resistant to treatment before the carbon dioxide is corrected and on loss of fluid from the intestine.

The author assumes some familiarity on the part of the reader with the essentials of electrolyte balance and gives abbreviated formulas for conversion and for diagrams. If the reader is not familiar with the constant acid-base equation in the body, he is stimulated to study the subject to determine the source of the figures. In one instance the author has used a chart and formula for the administration of sodium chloride after Coller and Maddock which has since been refuted by these authors. An actual calculation of the milliequivalents of chloride to be replaced on the basis of the blood plasma deficit and the body weight is a safer approach in this instance.

Dr. Aalkjaer has made a fine contribution to surgery in this monograph. In addition to the practitioner, every teacher of surgery in medical schools or hospitals should read this manual as a possible reference book for his students.

DONALD C. BALFOUR, JR.

IT is probable that relatively few physicians actively engaged in the practice of medicine today have the slightest conception of the travail and racking disappointments endured by our forefathers in attempting to systematize and organize the practice of medicine in the United States. The progress of medical development has lagged at times but it has always gone forward. Unfortunately, there are always some physicians who are more concerned with their personal welfare and progress than that of the profession as an organized entity. Nothing in organized medicine is durable or stable unless it unselfishly serves the welfare of mankind. As conditions of life change so must the concepts of organized medicine change, always keeping in the foreground the one salient objective—the preservation and restitution of health. There may be honest differences of opinion as to procedure. One man may be looking and planning far ahead of his time and his intellectual foresight may be extremely acute. Too frequently such an individual is ridiculed and his advice rebuffed. This is one of the unjust penalties that has been suffered by many, not only in the medical profession but in all scientific fields. The harmonious organization of the medical profession in the United States has been a tremendous task but it was no greater than the wisdom and efforts expended by the men who brought it about. This fact is well illustrated in *A History of the American Medical Association* by Fishbein.[2]

For interesting reading this book can be recommended heartily. Organized medicine may be just a bit behind the advance line of scientific medicine, yet it has followed medical progress very closely. Of necessity this must be so. It is just to say that organized medicine has never as a body strayed from a true scientific course as so many other organizations have. It has in the past definitely urged reforms and fought for principles deemed necessary to protect

[1] FLUIDS, ELECTROLYTES AND PROTEIN IN SURGERY; ACIDOSIS, ALKALOSIS, DEHYDRATION, CHLOROPENIA, PROTEIN DEFICIENCY, ANEMIA. SHOCK. By V. Aalkjaer, M.D. (Translated by Miss Annie I. Fausboll M.A.) Copenhagen: Einar Munksgaard, 1947.

[2] A HISTORY OF THE AMERICAN MEDICAL ASSOCIATION 1847 TO 1947. By Morris Fishbein, M.D. Philadelphia and London: W. B. Saunders Co. 1947.

human welfare. Repeatedly its demands have been carried to the door of the president of the United States. One cannot escape the question as to whether today the association is as virile and aggressive as it was 50 or more years ago. As early as 1852 the American Medical Association brought to light conditions to which steerage passengers in ocean steamships were subjected and demanded reforms. In 1854 dietary deficiencies in children were studied and an attempt made to correct conditions. In 1884 organized medicine was confronted by antivivisectionists and the situation was met as well as it is today, if not better. The first concrete attempt to curtail 4th of July accidents was made by the American Medical Association in 1903. It is a tragedy that the public has insisted on allowing ruthless destruction and maiming of our youth for sport, this in spite of years of admonishment.

Many of our medical forefathers considered honesty and genteel conduct an essential for the practitioner of medicine. In 1902 definite action was taken against fee splitting and solicitation of votes by one seeking office in the society. For many years the code of ethics was of supreme importance and much time was devoted to its development. We still must recognize that honesty in medicine is as important, if not more so, than unusual skill and learning.

This volume of approximately 1200 pages is divided into a number of sections. By way of introduction there is incorporated a very interesting sketch of the life of Nathan Smith Davis, the father of the American Medical Association. The first section gives data on the formation of the American Medical Association and the high lights of the numerous annual meetings. A section is devoted to the recipients of the distinguished service medal, one to biographies of the 101 presidents of the association, one to the councils and bureaus of the association, and one to publications of the association.

This book not only affords interesting reading but it is a storehouse of information on medical progress and organization. It depicts the characteristics of many men who for at least another century will be revered and honored as the fathers of American medicine.

JOHN A. WOLFER.

FIRST published in 1884, *Pye's Surgical Handicraft*[1] has progressed with the growth of medicine and surgery through 15 editions. The current edition by 44 contributors in England and Scotland and edited by Hamilton Bailey remains faithful to the endeavors of the original author. It continues to describe the details of surgical work as they appear from the viewpoint of the house surgeon and interne who must ever strive to become a skilled handicraftsman.

The volume is replete with excellent illustrations; many in full colors and some tinted in part. Unfortunately the selection of colored plates seems to have been somewhat haphazard rather than to fill a particular need. However, on the whole, the pictorial presentation of technical procedures is extremely informative and affords an unusual clarity of explanation.

Much of the book is devoted to the hospital care of surgical problems which are taken up chiefly in a regional manner. There is a slight but understandable lag behind the progress in certain fields, notably in the brief and inadequate references to chemotherapeutic agents and anticoagulants. Similarly, the chapters on the treatment of burns and the management of surgical thoracic cases have not kept pace with advances in these fields.

The American reader may encounter a few unfamiliar terms among the medications and dressings but this is not conspicuous and in no way detracts from the excellence of the text. It is packed with an abundance of practical points which will prove of great value to the surgical resident, interne, and student, and to the practicing surgeon as well. The reviewer recommends this volume most highly.

EDWARD W. GIBBS.

LIKE the modern hotel with a bath in every room, *Surface and Radiological Anatomy*[2] containing 300 pages has an equal number of illustrations. The second edition has been necessary to enlarge the text, replace all of the earlier skiagrams, and provide new surface illustrations. It is prepared for the student, who in his dissections, will find it useful to orient a knowledge of surface identification with the deeper parts which he is investigating. This splendidly illustrated book will also serve radiological and surgical fellows preparing for board examinations.

Far more radiological fundamentals could be added to advantage. Particularly commendable are the surface identification of blood vessels, nerves, and lymph glands and vessels. The book is obviously for students and for those who would refresh their memories later in practice. It is worthy of a larger distribution than it will achieve.

EDWARD H. SKINNER.

THE little book of 120 pages *A Short Handbook of Practical Anaesthetics* by Hoel Parry-Price[3] is written in refreshingly frank style characteristic of many British writers. It outlines the author's personal experiences and the lessons learned between 1920 and 1945 both in civilian and military practice. It will be found of real value by resident-anesthetists, and thoroughly experienced anesthetists will appreciate many of his points of view.

An interesting foreword, written by Mr. Cecil P. G. Wakeley, Consulting Surgeon to the Royal Navy,

[1] PYE'S SURGICAL HANDICRAFT: A MANUAL OF SURGICAL MANIPULATIONS, MINOR SURGERY, AND OTHER MATTERS CONNECTED WITH THE WORK OF SURGICAL DRESSERS, HOUSE SURGEONS, AND PRACTITIONERS. Edited by Hamilton Bailey, F.R.C.S. (Eng.). 15th ed. Baltimore: The Williams & Wilkins Co., 1947.

[2] SURFACE AND RADIOLOGICAL ANATOMY; FOR STUDENTS AND GENERAL PRACTITIONERS. By A. B. Appleton, W. J. Hamilton, and Ivan C. C. Tchaperoff. 2nd ed. rewritten by A. B. Appleton, M.A., M.D. (Cantab.), W. J. Hamilton, M.D., D.Sc., F.R.S.E., and G. Simon, M.D., B.Ch., D.M.R.E. (Cantab.). Baltimore: The Williams & Wilkins Co., 1946.

[3] A SHORT HANDBOOK OF PRACTICAL ANAESTHETICS. By Hoel Parry-Price, M.R.C.S., L.R.C.P., D.A. (R.C.S.). With a foreword by Cecil P. G. Wakeley, C.B. Bristol: John Wright & Sons, Ltd. London: Simpkin Marshall, Ltd., 1946.

contains the sentence "To my mind the anaesthetist is just as much a specialist as the surgeon, and should be rated as such." Surgeons in the United States might well consider this an authoritative statement.

RALPH M. TOVELL.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

CALCIFIC DISEASE OF THE AORTIC VALVE; A COMPREHENSIVE ANALYTIC SURVEY OF CALCIFIC SCLEROSIS. By Howard T. Karsner, M.D., and Simon Koletsky, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1947.

PRACTICAL OBSTETRICS. By Bruce T. Mayes, M.V.O., M.B., B.S. (Sydney), F.R.C.S. (Edin.), F.R.A.C.S., F.R.C.O.G. Sydney: The Australasian Publishing Co. Pty. Ltd., 1947.

TEXTBOOK OF THE NERVOUS SYSTEM; A FOUNDATION FOR CLINICAL NEUROLOGY. By H. Chandler Elliott, M.A., Ph.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1947.

ESSENTIALS OF PHARMACOLOGY. By Frances K. Oldham, M.Sc., Ph.D., F. E. Kelsey, Ph.D., and E. M. K. Geiling, Ph.D., M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1947.

ENDOGENOUS ENDOCRINOTHERAPY INCLUDING THE CAUSAL CURE OF CANCER COMPENDIUM. By Dr. Jules Samuels. Amsterdam: Holdert & Co., 1947.

PROBLEMS OF EARLY INFANCY. Transactions of the First Conference, March 3–4, 1947. New York: Josiah Macy, Jr. Foundation, 1947.

COMMUNICABLE DISEASES. By Franklin H. Top, A.B., M.D., M.P.H., F.A.C.P. and Collaborators. 2nd ed. St. Louis: The C. V. Mosby Co., 1947.

SYNOPSIS OF OBSTETRICS. By Jennings C. Litzenberg, B.Sc., M.D., F.A.C.S. 3rd ed. St. Louis: The C. V. Mosby Co., 1947.

TRATADO PRACTICO DE HEMOTERAPIA. By Dr. Emilio S. Sammartino. Buenos Aires: Vazquex, 1947.

CIRUGIA. By Rafael Urzua C.C. Santiago, Chile: Editorial Tegualda, 1947.

THE PRACTICAL NURSE. By Dorothy Deming, R.N. New York: The Commonwealth Fund, 1947.

GEORGE CRILE; AN AUTOBIOGRAPHY. Edited, with Sidelights, by Grace Crile. In two volumes. Philadelphia and New York: J. B. Lippincott Co., 1947.

ILLUSTRATIONS OF REGIONAL ANATOMY. By E. B. Jamieson, M.D. 7th ed. Section I: Central Nervous System; Section II: Head and Neck; Section III: Abdomen; Section IV: Pelvis; Section V: Thorax: Section VI: Upper Limb; Section VII; Lower Limb. Baltimore: The Williams and Wilkins Co., 1947.

PHYSICAL MEDICINE IN GENERAL PRACTICE. By William Bierman, M.D., with a chapter on Medical Rehabilitation by Sidney Licht, M.D., 2nd ed. New York, London: Paul B. Hoeber, Inc., 1947.

ARTIFICIAL PNEUMOTHORAX IN PULMONARY TUBERCULOSIS. By T. G. Heaton, M.B. (Tor.). 2nd ed. Toronto: The MacMillan Co. of Canada, Ltd., 1947.

ENGLISH-SPANISH CHEMICAL AND MEDICAL DICTIONARY; COMPRISING TERMS EMPLOYED IN MEDICINE, SURGERY, DENTISTRY, VETERINARY, BIOCHEMISTRY, BIOLOGY, PHARMACY, ALLIED SCIENCES AND RELATED SCIENTIFIC EQUIPMENT. By Morris Goldberg. 1st ed. New York, London: McGraw-Hill Book Co., Inc., 1947.

CORRESPONDENCE

PLASMA CLOT GRAFT OF PERITONEUM FOR PERFORATION OF THE STOMACH

To the Editor: In answer to the comments of Dr. Amos Koontz,[1] concerning my article entitled "Plasma Clot Graft of Peritoneum for Perforation of the Stomach," which appeared in the August, 1947, issue of SURGERY, GYNECOLOGY AND OBSTETRICS, I wish to reiterate, first, that the method described in my article is purely an experimental one. Second, I believe that it is the first time anyone has succeeded in closing a gastric perforation by an adhesive method entirely without the use of sutures. This method was devised only in the hope that it could help in a special type of gastric perforation, not the routine small perforation. In explaining the success of the last 4 of a series of 9 experimental animals, the technique of applying the grafts was extremely important because it also included a method of at least temporarily controlling the digestive action of gastric juice. The work of Virginia Frantz,[2] as well as that of many others amply demonstrated the local effect of oxycel when implanted in the body tissues. Since oxycel is an acid it is my belief that it served as a temporary block against the digestive action of gastric juice just as gastric mucosa does. The varying degrees of success met with, since the work of Neuhof[3] in 1917 and Koontz[4] in 1929 proved that a perforated hollow viscus under proper conditions could be closed with a suture patch successfully. Neuhof's method of autogenous fascial grafting and Koontz's method of ox-fascia grafting were both suture methods. My method differs from both in that it is nonsuture method, but is similar to Neuhof's method since it is an autogenous method using fascia-peritoneum for the posterior rectus sheath of the same experimental animal. No one denies the fact that the acidity of gastric juice is an important factor in its digestive action on tissue, other than gastric mucosa. This has been amply proved by Price and Lee.[5] But one must recognize the fact that fascia is one of the most resistant to this action. It was thought that if a combination of factors could be developed to delay the unusual digestive action of gastric juice enough to permit the growth of gastric mucosa across the site of perforation, the perforation might heal.

The healing that resulted was similar to that of those successful cases of suture patch grafting of Neuhof and Koontz. However, suture methods are not applicable in large perforations with widespread induration. In a series of 9 dogs, all were treated alike, before and after operation. Those with perforations that were sealed tightly by means of the oxycel plug, fascia-peritoneum graft, and pressure clamps were able to eat as soon as they recovered from their anesthetic.

Perhaps I may be able to indulge in a bit of self criticism in that no preoperative and postoperative gastric analyses were made. However, this was given considerable thought before beginning the experiment and abandoned. It was felt that, first, one had to prove that a nonsuture adhesive method could be used successfully in conditions approaching the normal, before an attempt is made to apply the method to the abnormal.

In the next series of experiments, we shall attempt to make closure on animals with Mann-Williamson ulcers that have been made to perforate with histamine in beeswax.

It is thought that oxycel, whose chemical name is polyanhydroglucuronic acid, blocks gastric acidity and therefore it has been used as a plug in the experiment.

Neuhof and Koontz in some of their experimental animals performed some form of short circuit operation at the time of grafting to control the hyperacidity. Koontz even inserted bismuth subnitrate into the stomach of some of his animals. Both methods appeared to aid in successful grafting by suture methods. Others have attempted the use of continuous gastric suction to successful conclusions.

By accentuating the mechanical technique involved in my method, the acidity of gastric juice was kept in mind, the use of oxycel as described being thought to block this activity.

Unlike Koontz's patch of ox fascia, Frantz and others have demonstrated that no local tissue reaction results from the use of oxycel. It has been shown that at the site of implantation of oxycel, multilocular nodules form, surrounded by a coagulated tissue membrane. As the oxycel becomes lysed and absorbed, the coagulation is surrounded by a zone of fibroblasts and invading large monocytes. Absorption is usually followed by connective tissue scar formation. It is quite noticeable at the time of implantation of the oxycel plug that, as it becomes moist, it swells thus filling the entire cavity at the site of perforation quite snugly.

Dr. Koontz, in his comment stated, "If the implant does remain intact however, the ultimate result is excellent." With this remark he helps to answer his own question. I believe that my successful experiments were due to the fact that my implants were placed in such a manner that they were able to remain intact and thus successfully produce healing of the perforation.

JOSEPH BLOOM.

[1] Surg. Gyn. Obst., 1947, 85: 155.
[2] FRANTZ, V. K. Ann. Surg., 1943, 118: 110.
[3] NEUHOF, H. Surg. Gyn. Obst., 1917, 24: 383–427.
[4] KOONTZ, A. R. South. M.J., 1929, 22:417–422.
[5] PRICE, P. B., and LEE, T. F. Surg. Gyn. Obst., 1946, 83: 61–72; ibid., 1947, 84: 959–961.